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A Weekly Journal of Science

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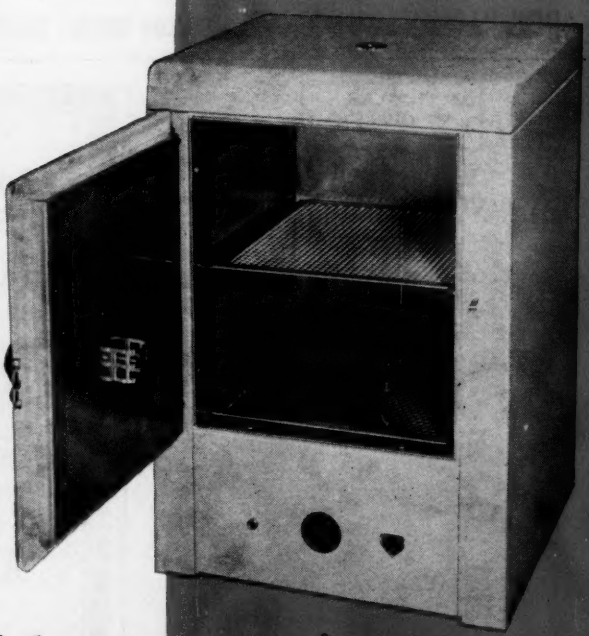

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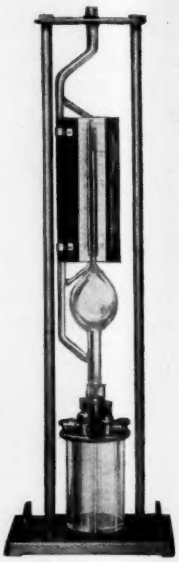

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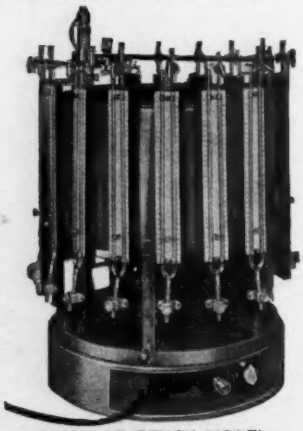

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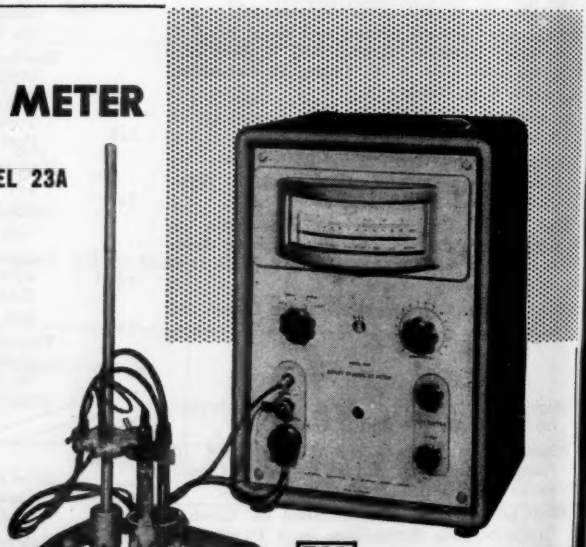

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RESEARCH IN THE UNDER-DEVELOPED TERRITORIES

"COLONIAL Research" continues to expand, although the report for 1957–58* is only some 25 pages larger than that for 1956–57. Apart from the brief annual report on Colonial research from the Colonial Research Council, it contains the thirteenth annual reports of the Committee for Colonial Agricultural, Animal Health and Forestry Research, the Colonial Medical Research Committee, the fourteenth annual report of the Colonial Social Science Research Council, the eleventh annual reports of the Colonial Economic Research Committee and the Colonial Pesticides Research Committee, the fifth annual report of the Colonial Products Council, the third annual report of the Colonial Road Research Committee and reports from the Colonial Fisheries Advisory Committee, the Tsetse Fly and Trypanosomiasis Committee and the Director of the Anti-Locust Research Centre covering the same period. There is also a report dealing with research matters such as building and housing research, the Falkland Islands Dependencies Survey, geodetic and topographical surveys, geological surveys, industrial and engineering research, and meteorology and water pollution research which are not covered by the accompanying reports of the specialist advisory bodies.

Some of these reports include as appendixes reports from Colonial or overseas bodies such as the East African Institute of Social Research, the Nigerian Institute of Social and Economic Research, the Rhodes–Livingstone Institute and the Institute of Social and Economic Research in the University College of the West Indies. There is also fully displayed the way in which the work in some fields can be linked with that of institutions in Britain, such as the Commonwealth Institute of Entomology, the Commonwealth Mycological Institute, Rothamsted Experimental Station, the Long Ashton Research Station, the Field Station at Silwood Park of the Imperial College of Science and Technology, the Unit of Experimental Agronomy of the Agricultural Research Council, and the Building Research Station of the Department of Scientific and Industrial Research. Nor is the impressive list of institutions mentioned in this publication exhaustive, for the recent report of the Nature Conservancy refers to help given by that body, notably in relation to a proposal to establish in Kenya a unit for research on wild fauna, and to the solution of controversy in Tanganyika over the reconciliation of practical problems and the scientific objectives of conservation in the Serengeti plains and the Crater Highlands. The Government's revised proposals here were closely guided by an ecological survey of the area undertaken by Prof. W. H. Pearsall on behalf of the Conservancy.

"Colonial Research 1957–58" thus provides an impressive, but even so, not exhaustive, picture of the effort which Britain is putting into research in the under-developed countries of the Commonwealth; and although the magnitude of that effort, either in terms of finance or of man-power, is not discussed directly, it is apparent that the demand for trained man-power is likely to have a far greater effect on Britain's limited resources than the demands of the under-developed countries for technical assistance have had in the United States, where it has already been cited as a contributory factor in the man-power shortage. The twenty-six new appointments made during the year brought the total complement of the Research Branch of the Oversea Service to 202 officers, and besides two continuing research fellowships, a further eight research studentships were awarded. Recruitment for moderately senior research posts continued to be difficult, but the Committee for Colonial Agricultural, Animal Health and Forestry Research reported more candidates for junior posts and awarded seven research studentships, bringing the total of research students to fourteen. The staff of the Colonial Section of the Road Research Laboratory reached sixteen during the year, but there are still nine vacancies. The staff of the geodetic and topographical surveys at the end of March 1958 was 437, and the overseas territories (excluding Malaya and Ghana) had 207 geologists, geophysicists and chemists on geological survey, with about twenty vacancies still existing, while meteorological work also was hampered by shortage of staff. It should be remembered, moreover, that the United Kingdom has already provided 317 experts under the Technical Co-operation Scheme of the Colombo Plan, an increase of 54 in 1957–58.

Apart from these items, "Colonial Research" gives no indication of the magnitude of the demand for man-power. Information on finance is equally sketchy. Expenditure under the Colonial Research Council during the year was £1,330,641 compared with £1,534,746 in 1956–57 and with £1,575,000 in the 1958–59 estimates. Colonial Development and Welfare Research Schemes made during the year brought the total allotted to such schemes under the Acts since 1940 to more than £18·5 million, of which £13·5 million has already been disbursed. Besides this, however, the United Kingdom has allocated since 1951 some £123·25 million for capital and technical assistance in the centres of south and south-east Asia under the Colombo Plan, of which £92·5 million had been disbursed by June 30, 1958

* Colonial Research 1957–1958: Reports of the Colonial Research Council; Committee for Colonial Agricultural, Animal Health and Forestry Research; Colonial Economic Research Committee; Colonial Fisheries Advisory Committee; Colonial Medical Research Committee; Colonial Pesticides Research Committee; Colonial Products Council; Colonial Road Research Committee; Colonial Social Science Research Council; Tsetse Fly and Trypanosomiasis Committee; Director, Anti-Locust Research Centre; and Research Matters not covered by the above Reports of the Specialist Advisory Bodies. Pp. 347. (Cmnd. 591.) (London: H.M. Stationery Office, 1958.) 14s. 6d. net.

(£3·71 million of this was for the Technical Co-operation Scheme). About 35 per cent of the gross allocation from Colonial Development and Welfare Funds has been for agricultural, animal health and forestry schemes, 16 per cent for medical research, 10 per cent for fisheries research, 9 per cent for tsetse and trypanosomiasis research, 8 per cent for social science and economic research, 8 per cent for pesticides research, 5 per cent for research sponsored by the Colonial Products Council, 3 per cent for anti-locust research and 6 per cent for miscellaneous schemes. About 38 per cent has been for schemes to benefit the East African territories, 16 per cent for the West African group, 12 per cent for the West Indian Colonies, British Guiana and British Honduras, 8 per cent for the south-east Asian territories and Hong Kong and 5 per cent for the central African territories.

Apart from this indication of the broad distribution of the research effort, the report really shows little of its relation to Britain's own effort. There is, however, a significant comment in the report on fisheries research during 1957–58. The Colonial Fisheries Advisory Committee points out that, with the closure of the West African and the Singapore fishery research stations, both regional and both considerably endowed from Colonial Development and Welfare Funds, Colonial fishery research appears to have entered a new phase, and that for some time to come fundamental research will be regarded in some territories as beyond their means. More and more research institutes will be asked to concentrate on applied research.

The Colonial Fisheries Advisory Committee recognizes the situation, and it is watching with interest a joint research and development scheme in Sierra Leone; but the difficulty should be considered in the wider context of an observation to be found in the recent report of the Secretary-General to the ninth meeting of the Scientific Council for Africa South of the Sahara. Here, too, is recognized the increasing importance of local factors; but the importance of basic research in a developing continent is firmly stressed, and while activities in the inter-African field are intended to serve the interests of Africa, in doing so the fullest support must be given to European research workers, institutes and technical departments. For a long time to come Europe will provide most of the scientific and technical assistance needed in Africa.

Rightly the report directs attention to the way in which the Scientific Council for Africa South of the Sahara is qualified to assist this evolution. Its members have been trained in the highest European disciplines and are eminent scientists who have devoted much of their lives to research. At the same time, they are all Africans, by adoption if not by birth, for their work and experience, their life itself, have for many years been in the service of Africa. The Council's meetings are held in Africa and its discussions and recommendations during the past nine years have had the sole objective of enabling science to assist the development of Africa.

There are already close relations between the Scientific Council and those engaged in Colonial research under the auspices of the various advisory research bodies the reports of which are collected in "Colonial Research"—for example, those concerned with fisheries or with social science; and the most cursory reading of either "Colonial Research" or the report of the Scientific Council for Africa South of the Sahara will show how much of the work is interrelated. It is indeed in this context that Britain's own effort in Colonial research is most appropriately considered. Valuable as the detailed work done by British and other European staff still is, it must be taken over more and more by trained men and women in the territory served as educational programmes develop. Meanwhile, however, and for years to come, the Colonial and similar territories will depend on assistance from the United Kingdom and other Colombo Plan countries, and from the specialized agencies of the United Nations; and the shortage of trained man-power throughout the world makes it imperative that there should be no hindrances to the efficient use of whatever scientific and technical man-power can be placed at the service of the under-developed areas.

This accentuates the importance of establishing the political and economic conditions, as well as the scientific and administrative means, for effective co-operation, and lends force to the contention of the Scientific Council for Africa South of the Sahara that it is essential to maintain an advisory group of highly qualified scientists, representing the various disciplines with which the Commission for Technical Co-operation in Africa South of the Sahara and the responsible Governments are concerned. Only as co-operation is promoted effectively at the highest level can we expect to ensure both the conditions for efficient scientific and technical work, and the removal of the obstacles that could, if allowed to remain, engender frustration and waste of effort, if not lead to real misunderstanding. The establishment last year of the Foundation for Mutual Assistance in Africa, stimulated largely by the success of the technical assistance programme under the Colombo Plan, both indicates the value of such co-operation and should in due course encourage the territories to provide their own scientific and technical experts, though the immediate effect may well be, by facilitating exchange, to increase the amount of technical assistance.

It is difficult at the present time to over-stress the importance of these matters not simply to science and technology but also to the economic future of Britain and the Western world. Sir Harold Hartley, in his Fawley Lecture last November, touched on its bearing on Britain's economic future and the challenge to industry to assist in developing the less-industrialized countries. He stressed the importance of careful planning, and indicated the extent of the demand for help which could reach even one company, as well as the difficulties which economic conditions and a narrow nationalist outlook could cause. In another context, Sir Oliver Franks, in his

chairman's address to Lloyds Bank, Ltd., referred to the dangers of allowing the gap between rich and poor countries to widen still further and to the policies that should be pursued to give effect to the undertaking to help the under-developed countries given at Montreal.

As Sir Oliver Franks points out, the under-developed countries cannot embark upon development programmes regardless of their own resources, and then demand that the industrial countries should underwrite them to any extent the under-developed countries wish. Nor is it reasonable to expect the under-developed countries, unguided, at this stage, to choose the right priorities in research, or to maintain a sound balance between fundamental and applied research, even if they could finance unaided the necessary programmes. It is at this stage, for years to come, that co-operation at the international level will be imperative, both in planning the programmes and in ensuring that the under-developed countries secure the maximum return from whatever resources in man-power, equipment and finance can be placed at their disposal through Colonial Development and Welfare Funds, the Colombo Plan, or the technical assistance programme of the United Nations.

There is still work to be done in creating the political conditions in which technical assistance is most effectively given, and much of the value of "Colonial Research 1957–58" lies in the conspectus it provides of the character and magnitude of Britain's effort in this field. It is important that this should be fully appreciated, particularly, in spite of Mr. Nixon's tribute to Britain's enlightened work, in view of the tendency to misrepresent colonialism. Some amplification of the picture as given in this report of the magnitude of Britain's effort in Colonial research in terms of man-power and finance, in comparison with the total research effort of the country and with the contribution of other countries to overseas research and development, might well be worth while including in future reports from the Colonial Research Council.

There is yet another aspect to consider. Under the Technical Co-operation Scheme of the Colombo Plan, the United Kingdom Government has provided the Pakistan and Ceylon Councils of Scientific and Industrial Research with scientific equipment for their laboratories at Karachi (£83,500) and Colombo (£80,000). Smaller sums have gone to the Plant Virus Research Laboratory, Manila, to the Soil Science Laboratory, Cambodia, and to the Agricultural Research Station, Kachim State, Burma. Such gifts all help to create the conditions in which effective scientific work is carried out, and the two thousand-odd trainees who have already been welcomed to the United Kingdom also help, on their return to their own countries, to promote the appropriate climate for research and development.

An even more important factor, however, may well be the conditions which already exist in the research institutions overseas, in the Colonial territories themselves and elsewhere. The standards maintained in such institutions must affect profoundly the quality of scientific and technical work in the territories they serve—for years to come and not simply while the work may continue to be carried out largely by scientists and technicians from Britain and other Western countries. The importance of the Colonial Research Council and of the various specialist advisory bodies, as well as of such bodies as the Scientific Council for Africa South of the Sahara, in this respect is not easily over-stressed and both from the reports on Colonial research and that of the Scientific Council for Africa, it appears that they are well aware of their responsibility. Nevertheless, "Colonial Research 1957–58" has a significance in this connexion which is not always appreciated. For many scientific workers engaged in research overseas, sometimes in comparative isolation, with slender opportunities for meeting their fellows, often in difficult or trying conditions, both technically and socially, the conspectus of scientific work displayed in the pages of this report represents one of the few opportunities which their work has of receiving attention. It is indeed a record of which British scientists have every right to be proud, and it might be worth while, both from Britain's point of view and that of recruitment to the Oversea Scientific Service, for closer consideration to be given to the possibility of giving more effective publicity to some at least of the many detailed achievements recorded in these three hundred pages.

QUANTUM MECHANICS IN ITS FOURTH DECADE

Quantum Mechanics

By Prof. H. A. Kramers. (Series in Physics.) Translated by D. ter Haar. Pp. xvi+496. (Amsterdam: North-Holland Publishing Company; New York: Interscience Publishers, Inc., 1957.) 45 guilders.

Quantum Mechanics

Non-Relativistic Theory. By L. D. Landau and E. M. Lifshitz. Translated from the Russian by J. B. Sykes and J. S. Bell. (Course of Theoretical Physics, Vol. 3.) Pp. xii+515. (London: Pergamon Press, 1958.) 80*s*. net.

Quantum Mechanics

By Dr. F. Mandl. Second edition. Pp. x+267. (London: Butterworths Scientific Publications; New York: Academic Press, Inc., 1957.) 35*s*.; 7 dollars.

Angular Momentum in Quantum Mechanics

By A. R. Edmonds. (Investigations in Physics, Vol. 4.) Pp. viii+146. (Princeton, N.J.: Princeton University Press; London: Oxford University Press, 1957.) 30*s*. net

Elementary Theory of Angular Momentum

By M. E. Rose. (Structure of Matter Series.) Pp. x+248. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1957.) 80*s*. net.

THIRTY-FOUR years ago, in 1925, quantum mechanics was born. The preceding twenty-five years had seen a gradual assembly of facts and a development of concepts which revealed startlingly the inadequacy of classical physics for describing

atomic phenomena, but not until 1925 could it be claimed that the new situation was understood. The great discoveries, associated primarily with the names of Heisenberg and Schrödinger, gave us this understanding in what in retrospect appears as one brilliant flash of insight. In fact, the period just after 1925 was one of intense theoretical development, to which many individuals contributed, and it was five or so years before quantum mechanics in the shape now familiar was completely revealed. The men who took part in this development have since stood out as the great figures of modern theoretical physics, and they and their immediate pupils have dominated the developments of the subject until very recently. Some of these men, indeed, still remain in the forefront of research. However, to-day a new generation of theoretical physicists is taking over, for which the nineteen-twenties are a chapter of history, and it is for these and their pupils that new text-books and monographs must cater. The mere passage of time must inevitably change a student's attitude to a subject of study. If one has grown up trained to think entirely in the language of classical physics, the transition to quantal thinking cannot but be a painful process, and in learning quantum theory one's main preoccupation will inevitably be with the 'paradoxes' it introduces, with the reconciliation of the new concepts and the old. But, just as the learning of a new language in infancy is a process entirely different from that of learning it in adult life, so the modern student can and should be enabled to acquire a working knowledge of quantum mechanics without having to live through the labour pains of its creators. True, one must insist on the fact that the very formulation of quantum mechanics requires the prior establishment of classical physics, but the initial teaching of classical physics can and should be adapted from the start to the quantal generalization to come, and quantum theory itself can be introduced with much less of a retrospective attitude. Many of the questions of the detailed relationship to classical theory may be left to a more advanced stage of development, just as grammar forms a later stage in the teaching of a language to a child.

To relegate to a secondary position the deeper studies of the foundations of quantum theory may seem unsound to many, but the reviewer feels that if to-day one's pupils are to be guided to the forefront of research in the limited time available for their training (and this time is limited not primarily by the educational system but even more by the inescapable fact that the peak in creative ability is so often attained at a very early age) changes in the directions suggested are inevitable. If we older generation of teachers do not make this re-orientation, our successors will certainly do so.

Of the five books the reviewing of which has given rise to these thoughts, the first, a translation of H. A. Kramers's classic contributions to the "Hand- und Jahr-buch der chemischen Physik", appearing as a single book under the title "Quantum Mechanics", is an example of the traditional exposition of the subject. In its class this work is undoubtedly one of the greatest. Kramers's part in the developments of the 'twenties was a more important one than is perhaps realized nowadays, and he was also one of the greatest of teachers. (To him we owe among so many other things the concept of 'renormalization' which dominated developments ten years ago.) The translator and publishers deserve nothing but praise for making this masterpiece available to English-speaking readers. Nevertheless, it is not a text-book one would nowadays recommend for initial study. In particular the reviewer cannot agree that the first five chapters, which also have been issued separately under the title "Foundations of Quantum Theory", are "extremely suitable as a text-book for college purposes" as claimed in the publishers' announcement. These chapters, while providing an admirable, one may say inspired, analysis of the relation of classical and quantal theory, do not even take the development as far as the introduction of spin.

A very different spirit pervades the volume on "Quantum Mechanics (Non-Relativistic Theory)", which forms part of the nine-volume course of theoretical physics by Landau and Lifshitz. This is again a translation, and as in the case of the preceding work the reviewer is disposed to praise translators and publishers wholeheartedly, passing over the quite minor blemishes noted in both works. The Landau-Lifshitz series is undoubtedly a worthy modern successor to the classic German series of Planck and of Sommerfeld and it is modern in precisely the sense called for in the introductory remarks. "Quantum Mechanics" is not the ultimate volume of the series, but the third. Only (classical) "Mechanics" and "The Classical Theory of Fields" are designed to precede it and, with "Statistical Physics" to round off the 'basic' disciplines, such 'derived' subjects as hydrodynamics, elasticity and electrodynamics of continuous media follow in later volumes. This conception seems admirable, and to judge from the volume in hand the execution matches the conception. To the serious student of theoretical physics no better text-book could be recommended, even though the Russian original appeared in 1947 so that certain recent developments (for example, 'effective range' theory in scattering) are inevitably missing and the emphasis on molecular theory is perhaps rather greater than one would desire to-day.

The third book on general quantum mechanics is the only original English publication of the three, Mandl's "Quantum Mechanics". This is a much less ambitious work, much shorter, more elementary and, let us be grateful, lower in price. We are told that the book originated in a course of quantum theory given to 'experimentalists' at Harwell in 1952 and one can see from the book why the course was a success. The author does a splendid job in making the ideas and methods of quantum theory clear with the minimum of mathematical sophistication. However, it seems to the reviewer that the very fact that such courses are needed in such a specialized centre as Harwell casts a sad reflexion on our British methods of training physicists. While in the Soviet Union it seems to be natural to place quantum mechanics side by side with classical mechanics and electrodynamics as a basic discipline in physics, here we have brought up the majority of our own physicists as 'experimenters' whose training, almost by definition, debars them from acquiring the language and tools of this branch of their subject at an early stage, so that they must seek enlightenment late in their careers in specially designed courses and in books in which mathematical argument of the slightest complication must be laboriously spelled out. How much better if Mandl's fine little book need never have been written!

A sign of the dominant role of quantum mechanics in modern physics is the need for specialized monographs on particular topics in the field. The two volumes on "Angular Momentum in Quantum Mechanics" by Edmonds and "Elementary Theory of

Angular Momentum" by Rose deal with one and the same such special topic. It is one that is included to some extent in any quantum mechanics text-book, but it has special importance in modern work, as these two monographs demonstrate, and is capable of being much expanded instructively and usefully. The difference between the two versions, which is considerable, seems to the reviewer to be just that in Edmonds's work the instructive character strikes one most, in Rose's the useful side. The latter author is himself responsible for a great many important applications of the methods here described, and in this monograph he has succeeded in bringing together in a unified form the mathematical theory underlying these methods as well as an extensive array of its applications, so that to future workers in the field the monograph will undoubtedly serve as a most useful manual. Edmonds in his shorter book lays relatively more emphasis on the formal and conceptual structure of the theory of angular momentum and his book is somewhat more of the nature of an expanded chapter of a text-book on general quantum mechanics. In fact, the Landau–Lifshitz volume contains an admirable chapter on this topic and the fortunate student who learns his quantum mechanics from that work will find himself fully equipped to master the further developments of this monograph. Edmonds's book will undoubtedly be appreciated by workers in the field not least because of the author's commendable policy of listing systematically and fully the great variety of symbols which, unfortunately, are in use to denote the various group theoretical coefficients in which the subject abounds.

N. KEMMER

PHYSICS FOR THE ELECTRICAL ENGINEER

Physical Basis for Electrical Engineering

By Prof. Thomas L. Martin, Jr. Pp. xii+410. (London: Macmillan and Co., Ltd., 1958.) 30*s*. net.

MOST engineers who have been out of college more than ten years, and many teachers of electrical engineering as well, will find food for thought in this book. Their first reaction may well be of dismay that it is now proposed to teach in a first course in electrical engineering (so the author suggests in his preface) a great deal of physics with which they themselves have only a slight acquaintance. After dismissing in the first two chapters the electromagnetic field *in vacuo* (from "Vectors and Scalars" via Poisson's and Laplace's equation to the Lorentz transformations and electromagnetic waves) the book goes on to describe modern ideas of atomic and nuclear structure, the structure of metals and of semiconductors, practical semiconductor devices, vacuum and gas tubes, dielectrics (including ferroelectrics) and the theory of magnetic materials.

Closer examination reveals the very real dilemma of the teacher of electrical engineering to-day. Wave-mechanics is carefully excluded from the book, and 'degeneracy' is not to be found in the index. Perhaps this is why the definition of Fermi-level in the text appears so inadequate that it has been supplemented by another definition in an appendix. But should one try to teach all these experimental phenomena, yet firmly refuse to dig in to the solid foundations? If there is not time to teach a student both physics and electrical engineering thoroughly, how valuable is a superficial account of the physics? Yet this is only the physical basis for to-day's electrical engineering—soon it will be yesterday's electrical engineering. (There is nothing here to help us understand the maser or the use of the concept of entropy in communication theory, for example.)

The extent of the work involved in writing a book which covers so wide a field as this book is not to be belittled, especially as it is fairly liberally supplied with references to original work to enable the reader to pursue his study of any particular point. But one does not need to be a specialist to pick holes in details. Among the dozen or so points noted in a quick reading, there is a suggestion on p. 185 that conduction in an intrinsic semiconductor commences "at some fairly definite temperature", and on p. 208 we are told there are semiconductor diodes and varistors and transistors, but on p. 210 "semiconductor diodes or varistors" appear to be one and the same. The treatment of space-charge-limited thermionic currents is not happy, and it seems clear that the author has neither read Langmuir's classic papers nor himself tried to measure accurately a 3/2-law characteristic.

To sum up, this book is a bold attempt to provide engineering students with knowledge of what the author considers to be the relevant branches of physics; but even the elementary student deserves a clear and accurate treatment of the topics, and there are some passages which are not up to this standard.

D. A. BELL

ANIMAL ECOLOGY

Animal Ecology

Aims and Methods. By A. Macfadyen. (Zoology Series.) Pp. xx+264+6 plates. (London: Sir Isaac Pitman and Sons, Ltd., 1957.) 40*s*. net.

THIS book is difficult to read owing to the use of multitudinous sub-headings which destroy the continuity of the chapters. Partly as a result of this, the treatment of individual subjects tends to be too slight: as soon as some topic begins to grow interesting, it stops short. It would have been better to have selected fewer subjects and dealt with them more thoroughly. Parts of the book are little more than a catalogue. On the other hand, the numerous references which this involves are certainly valuable, though their use is greatly impeded by the unfortunate device of splitting them up into fourteen separate lists at the ends of chapters instead of bringing them together to form a single corpus of literature.

The account of collecting methods (Chapter 6) is very brief and incomplete. Among other omissions, the mercury-vapour trap which has so much revolutionized our knowledge of the distribution and habitats of insects, especially the Lepidoptera, is not mentioned. The description of marking techniques is also too curtailed to be of use. It is condensed into a small paragraph on p. 89, and no mention is made of the exciting possibilities opened up by marking with radioactive materials (there is brief mention of their use in another connexion). The mathematical procedures to be used in marking – release – recapture work, which might certainly be expected in a book which sets out to include methods, are scarcely touched upon. One has the impression that the chapter on "Biocoenology" could advantageously be replaced

by one on ecological barriers, which are scarcely mentioned.

Yet though too many minor topics have been chosen, some important major ones are omitted. The ecology of marine and estuarine animals and communities, and the methods of studying them, are insufficiently described, while the vast contributions of ecology to the study of evolution are relegated to three pages. The theory of Sewell Wright is said to fall outside the scope of the book, though it is not clear why. It is mentioned in two brief paragraphs, in which it is said that "the existence of small isolated populations provides unusual opportunities for the rapid evolution of new sub-species bearing characteristics which would not be tolerated in the more normal conditions of larger populations among which natural selection is in full operation". It should also be pointed out that such conditions provide unusual opportunities for solution by natural selection. No attempt is made to include the great subject of ecological genetics, though we are told (p. 13) that "the genetic structure of a population in the wild is constantly changing, for it is the result of an equilibrium between mutation rate of recessive factors and selective elimination of unsuccessful individuals". It is very surprising that such a statement, overlooking polygenic variation and polymorphism, could be made in a modern book.

The captions on Plate 2 are interchanged, as are the two lower captions on Plates 5 and 6. The price seems high for a book of moderate size containing eleven tables, nineteen text figures, six black-and-white, and no coloured, plates. E. B. Ford

STUDY OF EARTHQUAKES

Elementary Seismology

By Charles F. Richter. Pp. viii+768. (San Francisco, Calif.: W. H. Freeman and Company; London: Bailey Bros. and Swinfen, Ltd., 1958.) 12 dollars.

At the present time, when geophysical methods and theories are permeating every branch of geology and geotectonics and effecting a gradual revolution in geological thinking, the appearance of a book which helps this process is an important event. Sound reasoning, likewise, in geophysics can only stem from a sound well-balanced basic knowledge of classical geology, physics and mathematics, ably synthesized as in the book under review.

This book is divided into three parts. Part 1, entitled "The Nature and Observation of Earthquakes", contains twenty-four chapters on 394 pages. The first fourteen chapters largely concern field observations of earthquake effects, the background for these chapters being geological and non-mathematical. Chapter 15 contains an elementary discussion of seismograph theory and practice, and there follow chapters on elastic waves, deep-focus earthquakes, and the reduction of instrumental observations. The final two chapters are on microseisms and on earthquake risk and protective measures to be taken in areas likely to be subjected to earthquakes.

Part 2 of the book is entitled "The Geography and Geology of Earthquakes" and contains nine chapters on 246 pages. The author of the book for many years has taken a very great interest in this work, and being thus exceptionally well qualified for the writing, cannot fail to be informative and stimulating. After an introductory chapter he sets off immediately into a discussion of arc and block tectonics, and follows this up with descriptions of the geotectonics and earthquake phenomena of California, New Zealand, Japan and Formosa. Most of these regions have been studied at first hand in the field by Dr. Richter, as also through the medium of instrumental data and literature. The part ends with chapters on the tectonic earthquakes of other regions; compressions and dilations; and on seismology in the U.S.S.R. Since the days of Prince B. Galitzin, Russia has been renowned for her students of seismology, and her sons to-day are worthy successors of this heritage (the late Dr. G. A. Gamburtsev; and Dr. E. T. Savarensky, Dr. D. P. Kirnos, Dr. V. I. Keylis-Borok, Dr. E. W. Karus and others).

Part 3 of the book, which contains seventeen appendixes on 100 pages, and is somewhat more advanced than Parts 1 and 2, being mostly composed of items useful in a seismological laboratory such as a list of seismological observatories, a table of angles of incidence of elastic waves in the Earth and related quantities for shallow-focus earthquakes; the refraction and reflexion of earthquake waves including the Zoeppritz equations; transit-time tables and magnitude charts. In addition, there are items frequently requested by the general public such as lists of large earthquakes, a chronology of historically important events and discoveries in seismology; and an appendix on earthquake-resistant construction.

As will be seen from the foregoing statements, the book is exceptionally well balanced, the proper weight having been given to field observations and geology. Within the limits set by the author it is comprehensive and even encyclopædic in its contents, being a masterpiece of selection and compression as only a practical seismologist and lively, experienced teacher could have accomplished. Since the book is so up-to-the-minute in its contents, however, one might have liked to see reference to recent experimental work on seismographs such as is being conducted at Stuttgart, Zürich and elsewhere—though perhaps the author includes this work in the list (on p. iv) of material abbreviated. However, there are very good lists of selected references by which anyone interested may pursue the studies so well begun.

The author, Prof. Charles F. Richter, is professor of seismology in the California Institute of Technology in Pasadena, California, where he has also worked for many years in the seismological laboratory with Prof. B. Gutenberg, Dr. H. Benioff and others. He is joint author with Dr. Gutenberg of the book entitled "The Seismicity of the Earth", and is an originator of the instrumental earthquake magnitude scale. For many years also Prof. Richter has been responsible for regular bulletins on local and distant earthquakes.

This book developed from a lecture course organized particularly for students of geology who do not intend to specialize in seismology or geophysics. Every geological library, and every geological student who can afford it, should get a copy of this book most opportunely published during the International Geophysical Year. It is lavishly illustrated and produced, and the printing, format and binding are all of the highest quality. The book is recommended not only to students of geology, but also to engineers and engineering students, applied mathematicians as a source book of data and ideas for problems, and to all others interested in seismology and the physics of the Earth. Ernest Tillotson

Proceedings of the Rehovoth Conference on Nuclear Structure held at the Weizmann Institute of Science, Rehovoth

September 8–14, 1957, under the auspices of the International Union of Pure and Applied Physics (IUPAP). Edited by Dr. H. J. Lipkin. (Series in Physics.) Pp. xvi+614. (Amsterdam: North-Holland Publishing Company; New York: Interscience Publishers, Inc., 1958.) 45 guilders.

THE Rehovoth conference of September 1957 will long be remembered by many who attended it, if only because it was their first opportunity to visit the young and fascinating State of Israel. Apart from that, the conference itself marks a certain stage of development of nuclear physics, a stage at which one feels that a qualitative and even semi-quantitative understanding of the structure of complex nuclei has been reached, and one beyond which must inevitably follow a period of consolidation. There is, in fact, some justification for the sentiment, sometimes expressed, that nothing much has happened in low-energy nuclear physics since the Rehovoth conference. There is, therefore, every justification for the appearance in print of the Proceedings of the conference provided in this handsome volume. The editor has been to great trouble to collate and edit the various communications, long and short, and has even included some carefully edited discussion. The sessions dealt with the shell model and the collective model and their foundations, group-theoretical methods in nuclear spectroscopy (including a beautiful introduction to the concept of seniority by Prof. Racah, who has contributed so much to the techniques of theoretical nuclear physics), electromagnetic properties of nuclei, beta-decay and parity violation, angular correlations in external fields, the instruments of nuclear spectroscopy, and the measurement of short life-times. A final section of the volume includes the *Daily Bulletin* of the Conference, which parodied and commented upon the actual proceedings with such delightful wit. In this permanent record of a memorable occasion the publishers have maintained their customary high standards of printing and presentation.

B. H. FLOWERS

Physical and Azeotropic Data

Hydrocarbons and Sulphur Compounds boiling below 200° C. By G. Claxton. Pp. v+146. (London: The National Benzole and Allied Products Association (N.B.A.), 1958.) 42*s*.

THE first part of this book gives the boiling points and densities of nearly 1,450 hydrocarbons and 190 organic sulphur compounds, together with the refractive indices of most of the substances listed and, in a few cases, melting points.

The second part describes the behaviour on boiling of about 1,000 binary, 90 ternary and three quaternary mixtures, azeotropic and otherwise. One component of every mixture is selected from twelve hydrocarbons and two sulphur compounds which are main constituents or impurities in coal tar benzoles. It is surprising, however, to find the benzene/ethanol azeotrope omitted from the list.

The first nineteen pages comprise a detailed explanation of the unusual system of nomenclature and classification used in the tables. These pages must be given careful study before the tables can be used, and the reader is not assisted by the incorrect printing of the four structural formulæ in Figs. 4 and 6, pp. 10–11. I would have preferred to see the standard nomenclature of the Chemical Society used in the book; the system is already widely known and leads generally to less cumbersome names than does that favoured by the author, and the reader would be spared the trouble of learning another system for which he will find no other use.

A few misprints occur, but the book should prove useful to all who use distillation for analytical or preparative separations and do not wish to use a more comprehensive work such as L. H. Horsley's "Azeotropic Data".

B. A. ROSE

The True Book about Insects

By John Clegg. (True Book Series.) Pp. 144. (London: Frederick Muller, Ltd., 1957.) 7*s*. 6*d*. net.

THIS is not another book on identification, but one bringing together information—often to be found only in specialist or out-of-the-way works—on many of the fascinating aspects of insect life.

It describes briefly the general structure of insects and how they grow, with chapters on flight, respiration, the senses of sight, smell and hearing, on feeding, colouring and camouflage. There are interesting accounts of such subjects as plant galls, with life-histories of some of the insects concerned; life in water, with its special problems of breathing and movement; the nuisance to man caused by insects which feed on his crops or transmit diseases, and the remarkable ways of the social bees, wasps, ants and termites. A chapter is included on the use of insecticides in the struggle against pests, with mention of some of the ventures in biological control. Illustrations are good line drawings, and there is a short list of books for further reference.

The author has chosen examples for his text from well-known insects from overseas as well as Britain, and his simply written and enthusiastic account will make a good introduction for the young student of entomology.

B. D. MORETON

Perkin Centenary—London

100 Years of Synthetic Dyestuffs. (Supplement No. 1 to *Tetrahedron*.) Pp. xii+136+8 plates. (London and New York: Pergamon Press, 1958.) 42*s*. net.

THIS book, to which Sir Robert Robinson contributes a foreword, provides a permanent record of the proceedings of the Perkin centenary celebrations. Besides the four Perkin centenary lectures, by Prof. John Read, Mr. C. Paine, Mr. J. G. Evans, and Sir Alexander Todd, it includes the speeches made at the Perkin banquet, details of the committees which planned and organized the celebrations, and the final financial report of the Perkin Centenary Fund, with a list of contributors to it. There are some interesting plates of Perkin himself, the Royal College of Chemistry, Hofmann and his students and the Greenford Green works. Prof. J. Read has put us further in his debt by appending to his own vivid survey of the life and work of Perkin references to some other papers on Perkin published at the time of the centenary or afterwards. The completeness thus given to the volume is a further reason for regretting that, while its production is worthy of such a notable event, the volume has not been produced in a style which would place it within the reach of a much wider range of chemists and general readers to whom its present price may be prohibitive.

R. BRIGHTMAN

THE THEORY OF NATURAL SELECTION TO-DAY*

By Prof. J. B. S. HALDANE, F.R.S.
Indian Statistical Institute, Calcutta

WE constantly hear that Linnæus is out-of-date, that his ideas are a danger to clear thinking, and so on. Why, then, do we not relegate them to a place in the history of science, like those of his contemporary Scheele on phlogiston? The answer is quite clear. Whatever we may think of Linnæus's theories, we continue to use his methods. In science, methods are much more important than theories, because a theory is an attempt to describe reality in terms of symbols made by the human vocal apparatus or on paper. If we think that the properties even of an electron are inexhaustible, theories can never be adequate. But a method, that is to say, a way of dealing with reality, may be adequate for the purpose for which it was designed, even if it is based on a false theory. The transition from a fluid to a particle theory of electric conduction in metals, and the partial return to a degenerate gas theory, had no effect on the design of galvanometers.

Linnæus invented the method of describing every animal or plant in terms of two, and only two, words. A group sharing the same two names is called a species. A group sharing the first only is called a genus. Genera are grouped together in higher categories, such as families, orders, classes and, more recently, phyla.

It is worth comparing this with some other methods of classification. To identify a particular star we give its right ascension and declination. In order to group stars which are judged to be similar, we use another two-dimensional classification. One co-ordinate is the surface temperature or a character highly correlated with it, such as the spectral type or colour. The other is the absolute luminosity. We then find that stars which agree in both these respects usually agree in others, for example, their period if they pulsate, their probable age, and so on. Linnæus tried such a two-dimensional classification of flowering plants, and it was one of his least-valuable contributions to biology.

The Linnæan system of classification is much more valuable in the tropics than in temperate or arctic climes, for the simple reason that there are many more different species of animals and plants. Linnæus's flora of Lapland was probably fairly complete. I am sure that nobody supposes that we have yet a complete list even of the flowering plants, let alone the ferns, mosses and liverworts, of Malaya. So it is no reproach to tropical biologists that they are still at the Linnæan stage when those of temperate climates have gone beyond Linnæus. One might as well reproach students of proteins because they cannot yet describe the structure of proteins with the accuracy possible for sodium chloride. It is therefore entirely fitting that we should be commemorating Linnæus on the equator.

If Linnæus's method of assigning every living organism to a species is so useful, why do we attack his species concept? The species concept, like the concept of a molecule, is not always true; but even where not true, both can be useful. Sodium chloride does not exist as molecules either in crystals or in solution. But it is convenient to use the same terminology to describe sodium chloride and carbon tetrachloride, though the latter is a true molecule. Similarly, we can describe a silicate the anion of which is a lattice of indefinite extent in terms appropriate to a small molecule. By the end of this century I expect that our chemical vocabulary will be brought up to date. I do not think the Linnæan terminology will be abandoned for several centuries.

The Linnæan species concept often breaks down when we extend our studies over a large enough space. Classical cases are the circum-Tibetan distribution of *Parus* and the circumpolar distribution of *Larus*. Here differences, which are at best subspecific, add up to a specific difference. The principal postulate of evolutionary theory is that all, or almost all, specific differences disappear if we trace the ancestry of two species far enough back. Thus, the horse and ass are believed to be descended from one ancestral species in the Pliocene, the horse and any bird from a common ancestral species in the Carboniferous. Finally, recent work on the transfer of substances (perhaps always deoxyribonucleic acid) responsible for hereditary differences, between bacteria not only of the same but also of different species, suggests that the species concept is only roughly applicable to bacteria.

But most biologists, and particularly experimental biologists, are dealing with organisms living in the present and obtained in a particular locality. The determination of their Linnæan species is a prerequisite to description of other observations. It may be said that the Linnæan system is merely a convenience of human communication. This is perhaps true, but it raises the question whether any scientific theory, or for that matter any philosophical theory, is anything more than such a convenience.

It is not a trivial fact that Linnæus worked on the periphery of the area where science was studied in his time. This meant that rather few of the plants and animals of his native country had been described either by the scientists of the ancient Mediterranean culture such as Aristotle and Theophrastus, or by such men as Aldrovandus and Gessner. Two centuries earlier, when Britain was similarly peripheral, Turner had realized that the plants and animals of his country required special study and special names.

It is not trivial that Darwin and Wallace were stimulated to formulate the theory of evolution as they did by observing the plants and animals of countries very distant from their own. A four-year voyage around the world gave Darwin enough facts inexplicable without a theory of evolution to last him a life-time, but in his case the theory germinated slowly. Wallace had spent much longer in the tropics, and produced a theory equivalent to Darwin's in a shorter time. It is not impossible that some resident in a scientifically peripheral area such as Singapore or Calcutta may to-day be making observations

* Substance of the presidential address delivered at the Centenary and Bicentenary Congress, University of Malaya, Singapore, on December 2, 1958. (See also p. 723.)

which will form the basis of an advance in biology comparable to those made by Linnæus two centuries ago, and by Darwin and Wallace a hundred years since. I shall later suggest reason to hope that Calcutta may be the locus of such a discovery.

Darwin and Wallace not only championed the notion of evolution, but also produced a coherent theory as to how it had occurred. To-day almost all biologists believe in evolution, that is to say, they believe that the plants and animals alive to-day, including men, are descended from ancestors very unlike themselves, and that many very different living forms are descended from one ancestral species. However, by no means all living biologists believe that the main agency of evolution has been natural selection. Indeed, Wallace in his old age concluded that a decisive step in the evolution of man could not be so explained.

Darwin thought that evolution occurred by imperceptibly small steps. To-day we know that some of the steps have been fairly abrupt; and this is the main modification to which the account of evolution given a century ago must be subjected. These steps are of three main kinds. Mendel showed that on crossing races of peas certain characters showed no blending. Even when a character disappeared in the first generation it might reappear in a fraction of the next. We know that some evolutionary steps are due to the selection of characters inherited according to Mendel's law. About seventy species of British Lepidoptera have evolved black varieties since the industrial revolution, and some have almost completely replaced the original light form in the smokiest areas. In the best-studied case, *Biston betularia*, the dark form differs from the light by a single dominant gene. I shall later describe why the population evolved as it did. At present I merely wish to point out that the evolutionary process was not gradual, in the sense that the population did not pass through a phase of intermediate colour.

Secondly, the chromosomes, on which the genes responsible for Mendelian inheritance are carried, change abruptly. The number in a species is usually constant, and must be an integer, usually an even one. Not only does the number change, but also when a new species evolves, parts of two different chromosomes can be exchanged, so that in the hybrid the normal process of gamete production by meiosis is disturbed. This is not the only cause of hybrid sterility, perhaps not the main one, but it is one cause of this important biological fact.

Thirdly, and most important, we now know that a new species can arise in one step by the formation of a sterile or nearly sterile hybrid followed by a doubling of the chromosomes which renders it fertile but still vigorous. Such hybrids, which are called allopolyploids, breed very nearly true. While Winge and others must take much credit for this discovery, the most decisive steps were probably taken by the Japanese botanist Kihara, who recently crowned his life's work by discovering growing as a weed in wheat fields in Afghanistan the grass which, by crossing with a wheat like the macaroni wheats of to-day, gave rise to the bread wheats in or near Afghanistan about 6,000 years ago. It is probable that Kihara has made the most important amendment to Darwin and Wallace's account of evolution as a historical fact.

Finally, Garstang, Bolk, de Beer, and others have pointed out an evolutionary process at which Darwin and his immediate successors had not guessed. Many animals pass through a larval stage, and this may be highly specialized for its own kind of life. You have only to think of such familiar larvæ as a caterpillar and a tadpole. If the timing of development is shifted so that reproduction occurs when some or most of the non-reproductive organs are still in the larval stage, this may lead to the evolution of a wholly new adult type. Such are, for example, the Larvacea, or swimming tunicates, which resemble the larvæ of the sessile forms, but never attach themselves to rocks. It is probable that the Copepod Crustacea, a very successful order, are essentially larvæ of prawns or crabs which never grow up. A similar process has played a great part in human evolution. The development of our nearest relatives is very slow. A chimpanzee is not mature until about eight years. A human being is not mature until about sixteen, and never develops many of the characters of adult apes, let alone adults of other mammalian groups. In particular, we have kept the embryonic character of cranial flexure, so that our eyes are directed forwards and not upwards or even backwards. A change in the timing of sexual maturity may occur quite suddenly, as it does in the axolotl, and have very great evolutionary effects.

Nevertheless, palæontological research has, on the whole, fully confirmed Darwin and Wallace. Among the more spectacular 'missing links' which must have lived if their account of evolution is substantially correct, and are no longer missing, though they were so in Darwin's time, are amphibians with four legs but a fish-like tail with bone-supported fins, birds with long tails, teeth, and many other primitive features, and later short-tailed but still toothed birds. Our picture of vertebrate evolution is now so complete that one can make a list of dozens of discoveries, any one of which would go far to disprove the theory of evolution. For example, if the skeleton of a man or a horse were discovered in the Cretaceous, or that of a reptile or a bird in the Devonian, I, for one, would regard most of my life's work as having been as futile as that of an astrologer. Every year in which such discoveries are not made strengthens the evidence for the theory of evolution, and makes it less possible for biologists to accept any other theory.

Although both Darwin and Wallace made major contributions to the study of variation (and Darwin did some very important genetical work), we now know so much more than they did on these matters that their account of how evolution occurs must be restated. In my opinion, most of what they wrote is true; but the fact that they reached the truth on the meagre evidence before them is a proof of their genius.

Let me try to state the theory of natural selection as I hold it in language which they would have understood. "All species vary. But not all variation is inherited. Natural selection discourages most variations from the structures and functions normal in a species. It encourages a few variations; and if these are inherited, evolution will take place."

The main objection to this formulation is to the word 'inherit', which is applied to property and to characters. For example, I have inherited my father's watch, his baldness, and a growth of bristles on the nose. We could not both possess the watch simultaneously, but we were simultaneously bald. It may be incorrect to speak of possessing baldness, but we certainly possessed the nasal bristles simultaneously. A character is not an object like a watch, and it is misleading to use the same word about it.

The physical basis of heredity is now fairly well understood. Certain patterns in cells are copied with great fidelity when a cell divides. The most important are the molecular patterns which we call genes, and which determine what kinds of proteins will be built in the new cells, and thus may have a great effect on the structure and function of descendant cells and organisms. However, a character, such as tallness, hairiness, or capacity for distinguishing between green and grey, can only be said to be inherited if it depends in a fairly simple way, either on genes in the nucleus, or on the rarer copiable molecular patterns outside the nucleus. A change in one of these copied patterns, whether it is due to copying error or alteration between copyings, is called mutation.

Heredity can be defined statistically as a positive correlation between characters in a group of ancestors and their descendants, which is not due to a positive correlation between the environments of ancestors and descendants. My skin colour is hereditary in the biological sense, my linguistic habits are not. My mother taught me to speak English; but if I had been handed over to a Malay foster-mother as an infant, I could just as easily have learned to speak Malay.

An example of a biological and genetically determined character which is not inherited is the complete sterility of some so-called double-flowered plants such as the double *Matthiola incana*. Other characters, such as size within a pure line, are not inherited, because they are not genetically determined any more than are human languages.

Natural selection may be defined as a statistical difference between the parents of the next generation and the population from which they are drawn, each parent being counted once for each of its progeny. Darwin and Wallace thought mainly in terms of selection by survival, but fully recognized selection by fertility, parental care, and other means. We now see that selection, whether natural or artificial, is not always effective. For example, roan cattle (which, by the way, are common in England and very rare in India, though they exist, but may be unknown in Singapore) do not breed true, and selection in favour of roan may increase the frequency of roan to about 50 per cent, but cannot raise it above this level.

But as soon as biologists began to study natural selection they found something much more surprising. Natural selection is generally centripetal, that is to say, it favours individuals near the norm of the population in question, at the expense of those which deviate from it. In other words, the parents of the next generation are usually less variable than the generation of which they form a part. This is difficult to prove formally, because one cannot often determine parenthood in animals or plants under natural conditions, but it has been abundantly proved for many episodes of selection by killing. Perhaps the first case was Bumpus's observation in the late nineteenth century that of a number of sparrows picked up immobile with cold after a blizzard, those which did not recover were more variable in several measurable characters, such as wing-span, than those which did.

In the human species, centripetal selection occurs at all stages. For example, babies which are lighter or heavier than the average have a higher death-rate than the average. So have adults with very high or low weight or systolic pressure. When it comes to intelligence, the very stupid, who are classed as mental defectives, have a much higher death-rate than the average, and the survivors are less fertile than others, as they are largely confined in special institutions or in prisons. The very intelligent are probably longer-lived than the average, but are less fertile.

Centripetal selection acts partly by eliminating mutant genes, and partly by eliminating homozygotes, that is to say, organisms which have a like pair of genes, instead of an unlike pair, in a particular region of a chromosome. Thus, the first observations certainly confirmed Darwin and Wallace that natural selection occurs, but showed, contrary to their belief, that its main effect was to prevent species from changing. Only much later was natural selection with an evolutionary effect discovered.

The reason for this is clear enough. Evolution is a very slow process, how slow only Darwin guessed. He estimated the age of the Wealden, or upper Jurassic, at about 300 million years. His contemporaries, if they believed the theologians, put it at 6,000 years; if they believed the physicists, at about a million. The correct figure is about 130 million. In a fairly steadily evolving line such as the ancestors of horses, the average rate of change of a character, such as length of tooth, is about 4 per cent per million years. In 1924 I calculated the intensity of selection needed to make such changes. An advantage of one-thousandth for one type over another would be much more than enough; and this could only be detected on a sample of several millions, whereas a 10 per cent advantage could be detected on a sample of a few hundred.

In fact, natural selection with evolutionary consequences has only been observed where men have created drastically new conditions which impose a heavy selection pressure. The most striking is the use of insecticides such as DDT. This causes intense selection in favour of resistance to it, and relatively resistant races of mosquitoes arise in a few years. The best-studied case is that of the moth *Biston betularia*. In the smoke-polluted parts of Britain the original light form is conspicuous when resting on tree trunks, as these moths do during the day. In the unpolluted areas the dark form is equally conspicuous. Kettlewell found that birds ate the form which is conspicuous to human eyes at such a rate that if equal numbers of the two forms are released at dawn, the ratio of inconspicuous to conspicuous moths caught in flight the next night is 2 : 1. Thirty years earlier I had calculated, from the rate at which the numbers of the black form had increased, that the fitness of the light form in smoke-polluted areas was about 70 per cent of that of the black. This may well be true on an average, for Kettlewell chose a highly blackened wood near Birmingham for his experiment.

I have no doubt that natural selection of much less intensity, but yet with an intensity far greater than that which has been usual in the past, is going on in many species. But it would be difficult for a single worker to collect the data.

Can natural selection explain evolution? If Darwin thought that it could, this was perhaps because he thought that members of a species varied in all possible directions, and natural selection could favour any kind of variation. This is probably not so. Only certain kinds of heritable variations seem to be possible in any particular species. The course of evolution is not (except perhaps in very rare cases) determined by the frequency with which a

particular type of mutation occurs; and the vast majority of mutations are rejected as useless, the process of rejection being called centripetal selection. No important event has only one cause. Houses would not be burned down if they were all made of ferroconcrete, or if the air only contained 17 per cent of oxygen. If there were no mutation, natural selection would be ineffective; if there were no natural selection, every species would become a collection of freaks. Only in this rather restricted sense can it be claimed that natural selection explains evolution.

However, it does not follow that the claim is true. In contradistinction to Wallace, I think it probably is true. Let us take such an organ as the eye of a man or a bird. It has been argued that it could not have evolved by natural selection, because it would seem that any improvement, in the later stages at least, would require simultaneous changes in several of its measurable magnitudes. I think a careful study of the eyes of living molluscs greatly weakens this argument, as we can find among them a dozen or so stages from a mere light-sensitive spot to an eye with a lens and retina much like our own. Wright has shown how, in small animal or plant communities, several changes, each slightly harmful, but beneficial in combination, may occur together.

Wallace regarded the origin of certain characters which he considered to be specifically human as inexplicable by natural selection. Many such characters, including a disposition to monogamy and a respect for property, both of which human moralists might envy, have since been found in animals. I have also shown, or at least suggested, how a mode of behaviour originated by the initiative of a single individual, and then converted, by imitation, into a tradition, may become instinctive as the result of natural selection. Until it has been shown that my arguments are worthless, it may be rash to say that natural selection cannot account for such changes. It is equally rash to assert dogmatically that it can.

If this celebration were merely concerned with eulogies of three great men, it would be worse than useless. If it helps us to imitate them, it is of the greatest value. Linnæus, Darwin and Wallace had this in common, that they did not use complicated apparatus. Any student to-day would turn up his nose at Darwin's microscope. Now we in India find it difficult to get apparatus. This discourages us from some lines of biological research. We cannot get electron microscopes, highly purified amino-acids, and so forth. But we can get land and labour to grow plants or keep animals, we can collect them on a large scale, and we can at least travel all over India. I want to tell you what I am trying to do in these circumstances.

I have already acted as a catalyst in getting one of the world's leading palæontologists (Dr. Pamela L. Robinson, University College, London) over here; and, with Indian colleagues, she has, in about ten weeks work, obtained reptilian and fish fossils, some of which are new to science, while others date some mesozoic formations with considerable precision (*Nature*, 182, 1722; 1958). Similarly, I hope shortly to catalyse the visit of one of the world's leading systematists to attack a group of animals the Indian representatives of which are practically unknown. My own junior colleagues are at last continuing the study of variation where Karl Pearson and Bateson left it fifty years ago.

Perhaps I may begin with a discovery made by a colleague, Mr. K. Dronamraju. Darwin directed attention to heterostylism in *Primula* and other genera. In many species there are two types of plant, in one of which the flowers have long styles, in the other short. The position of the anthers also differs. The phenomenon is called heterostylism. Darwin found that crosses between flowers of the different types gave far more seed than the so-called illegitimate unions between plants of the same morphological type. As no work of this kind has been done in the tropics, I asked Mr. Dronamraju to look for a suitable plant near the Indian Statistical Institute; for the assessments of fertility and of the viabilities of seeds in such cases raise some interesting statistical problems. Mr. Dronamraju discovered something much more important. He found both long-styled and short-styled flowers growing together on each of five trees of *Bauhinia acuminata*. So far, his results are merely statistical. In a year or two I hope that he will have physiological results also. This observation would most certainly have excited Darwin, who did not attempt to hide his emotions, so that his books are full of such adjectives as 'wonderful' and 'beautiful'. It is at least possible that heterostylism started as a variation between flowers on the same plant, and that, later, genes which controlled it were evolved.

Another colleague, Mr. S. K. Roy, is also almost slavishly imitating Darwin's interests. He has measured the amount of earth brought up by earthworms in Bengal and Bihar, and his measurements are the first to be made in Asia. A proper understanding of Asian soils demands that they be repeated in a thousand different places. I hope that some will be in Singapore or Malaya. He is now working, among other things, on variation in the like parts of the same plant. In a number of individuals of three different species he has reached the startling conclusions that while the mean number of petals per flower does not alter much during a season, the variance usually increases, and may be doubled. If the size of pots made by a potter became more variable at the end of a day, we should say that he was getting tired. I do not know what we are to say about a plant. To reach this conclusion, Mr. Roy has examined about 200,000 flowers. It is an interesting coincidence that Dr. A. K. Sharma, with his wife and other colleagues in the University of Calcutta, are working on differences in chromosome number in different organs of the same plant.

The point which I want to make is this. Apart from genetics, which can scarcely be understood without some special knowledge, no work is going on under my supervision which Darwin or Wallace would not have readily understood, and which is not, in fact, a continuation of a line of work started by one of them. Nevertheless, most of it is original in the sense that it is not an attempt to extend to tropical animals and plants principles which have already been established as holding in Europe, North America or Japan. It was Wallace, above all, who saw that certain biological problems are forced on one by a study of tropical life, which are by no means so obvious in temperate climates. The converse is, of course, true. Many ecological questions are fairly simple in the arctic regions, where a biotic community may consist of only twenty or thirty species; more difficult in the temperate zone, where a hundred or more species must be considered; and extremely complicated in a tropical rain forest, where it might be necessary to consider thousands of species, many as yet undescribed.

RIVER FLOW IN GREAT BRITAIN, 1955–56

By Prof. DAVID L. LINTON
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HYDROMETRIC statistics derived from regular measurements made at gauging stations on British rivers were first published by the Ministry of Health in 1938 and then lapsed during the War. Two volumes, published in 1952 and 1955, each covering eight years, brought the record (in a condensed form) up to 1953. "The Surface Water Year Book of Great Britain, 1955–56" (H.M.S.O. For the Ministry of Housing and Local Government, 1958. 15*s*. net) is the third in the new series. [It has been followed after a short interval by the fourth of the series, dealing with the period 1956–57.] The volume for 1955–56 contains results derived from 128 gauging stations maintained for a variety of purposes by river boards, water-supply undertakings, county councils, hydro-electric authorities, and others, and gathered together by the Surface Water Survey. For a minority of stations the records are incomplete or defective in some respect; but for the great majority we are given for each month of the hydrological year (October 1955–September 1956) the observed mean rate of discharge in cusecs (cu. ft./sec.): the gross mean (or natural) rate of discharge (in which allowance is made for additions or abstractions for reservoir, canal or hydro-electric purposes); the highest and lowest mean daily rates of discharge in cusecs, and the highest observed rate of discharge in cusecs however brief its duration, together with the date of its occurrence. From these data two further quantities are derived and tabulated for each month, namely, the gross mean discharge per square mile of catchment area, and the 'run-off', while the rainfall received in each of the twelve months and the corresponding mean monthly rainfalls are added for comparison. Finally, appropriate yearly rates or totals are quoted and some data are supplied concerning the location and character of the gauging station, the extent and hydrological character of the area draining to it, and the length and nature of the record.

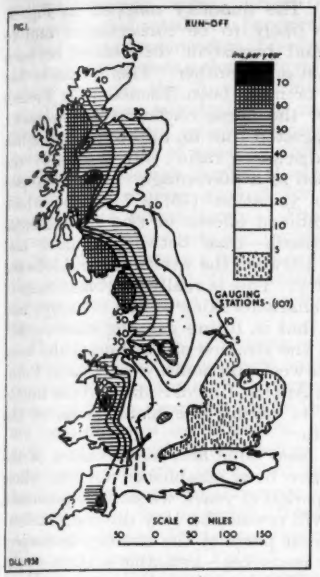
Examination of the tabulated figures does not need to be very prolonged to reveal that the Tay is the most copious river of Great Britain. Its mean rate of discharge of 4,146 cusecs for the water year 1955–56 (and of about 4,000 cusecs over a ten-year period) at Caputh, where it emerges from the Grampian Highlands after draining 1,238 square miles, is not even approached by any rival. The Ness outflow of Loch Ness yielded 2,574 cusecs, and the Spey at Aberlour 2,188 cusecs from 692 and 1,020 square miles, respectively, and these figures differ little from longer-period averages. The figures for the 1955–56 mean flows of the Thames at Teddington (3,810 square miles), the Severn at Bewdley (1,650 square miles) and the Wye at Cadora (1,560 square miles) were 1,811, 1,557 and 1,806 cusecs, but longer-period averages of 2,373, 2,285 and 2,484 cusecs, respectively, are quoted. Maximum flows for a single day follow a similar order: in 1955–56 they were for the Tay 31,500, Ness 12,000, Spey 20,000, Thames 10,700, Severn 13,200 and Wye 13,900. Over longer periods higher rates of flow have been recorded or estimated, namely, Tay 42,000; Ness 20,900; Spey 27,000; Thames 27,900; Severn 23,000 and Wye 32,000. Some other rivers have had high flood flows, and the figures of 40,000 cusecs for the Aberdeenshire Dee at Woodend from 220 square miles; of 16,800 cusecs for the Welsh Dee at Erbistock from 401 square miles; and 21,000 cusecs for the Irwell in Manchester from only 226 square miles, are notable.

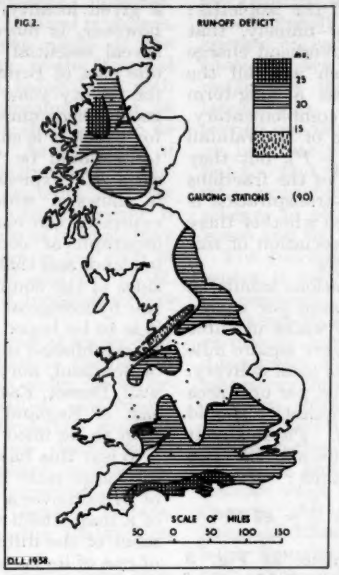
The Tay is the only British river for which the mean daily flow never fell to 1,000 cusecs during 1955–56. Minimum daily flows for the other rivers mentioned above were Ness 550, Spey 585, Thames 243, Severn 320 and Wye 312. Minimum flows for purely lowland rivers may fall to such very low values as 23 cusecs for the Great Ouse at Bedford or 21 cusecs for the Nene near Peterborough, because of high summer evaporation. For such rivers the ratio of the largest and smallest mean daily flows may be 80 or 90 to 1. For the Ness, on the other hand, it is less than 22, while for the Tay, Thames, Severn and Wye the ratios are 30, 44, 41 and 45 to 1. Very high values of this ratio are found for many small streams, of which 180 for the Monnow, 237 for the Medlom and 900 for the Essex Blackwater may be cited as examples.

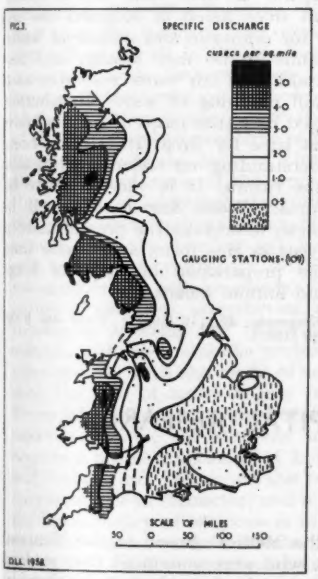
Since rates of flow are tabulated for each month of the water year, seasonal variations can to a certain extent be studied. Highest values are most generally in December, January and February, when evaporation and transpiration are at a minimum. Other high values may reflect either seasonal rainfall maxima in October and August normal to the areas concerned, or high discharges connected with particular rainy spells. Comparison of the flow records with the periods of heaviest rainfall tabulated in the pages of "British Rainfall" would doubtless be revealing. Since seasonal flow can be so dominated by spells of abnormally heavy rain, many years records will be required before normals of monthly flow can be established.

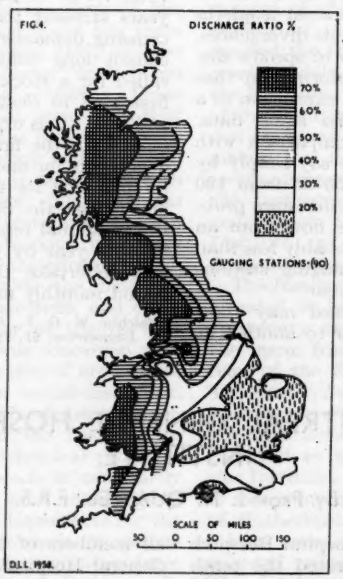
While the points mentioned above are evidently of interest, they do not lend themselves to any but the crudest comparisons of one stream with another. For more refined or more far-reaching analysis, cartographic treatment is necessary, and it is remarkable that nothing of the kind is attempted in the present volume. Four quantities which will here be called the 'run-off', the 'run-off deficit', the 'specific discharge' and the 'discharge ratio', are appropriate for such treatment. Of these, the first is tabulated for 107 gauging stations, and the third (though under another name) for 109; the other two have not apparently received any consideration by the Surface Water Survey; but they can readily be derived for the 90 catchment areas for which the total rainfall for the hydrological year 1955–56 has been supplied. The cartographic representation of these four quantities is shown in Figs. 1, 2, 3 and 4.

In the catchment basin of any stream above a selected gauging point, the rainfall received in a water year will, of course, vary from point to point, possibly quite widely; but if enough records are available an isohyetal map may be drawn and the mean rainfall (P) may be determined and expressed in inches. A sheet of water of that depth and covering









the area of the drainage basin would equal in volume the total rainfall received. Of this total, a quantity (Q cu. ft.) is actually delivered to the gauging station in the course of the year. This quantity deserves a name, and, it is here suggested, may best be called the annual 'delivery' of the basin. If the delivery (Q cu. ft.) be divided by the area (A sq. ft.) of the basin, the quotient is a quantity exactly comparable to the mean rainfall of the basin, and like it may be expressed in inches. This is tabulated for 107 streams as the 'run-off' (R), and its variation over a large part of Great Britain is shown in Fig. 1. It is thought that the features shown by this map for 1955–56 would strongly resemble those for any other water year, and that they are, therefore, worth a little discussion. The wide range of variation (the ratio maximum/minimum is 73/1·7 or 43) will at once be noted as greatly exceeding the range of mean rainfall (200/19 = 10·5) in the same area. Moreover, it will be noted that extreme high and low values prevail over larger areas than the extremes of rainfall. Almost the whole of the English Plain, which receives rainfalls of 20–35 in., has run-off values less than 10 in. a year, and over most of East Anglia, the Fens and the Thames Valley the values are less than 5. At the other extreme, large areas in western Scotland and Cumbria, and small areas in Wales and Dartmoor, yield an annual run-off in excess of 60 in., though no data are available concerning the run-off in western coastal districts. Between the extremes, values of R fall off sharply from west to east and the isopleths probably migrate eastward in wet years and westward in dry years, leading to marked year-to-year fluctuations in areas like Peebles, the West Riding, or Herefordshire. An interesting feature is the extension of quite low run-off values as far as Chester in the rain-shadow of the Welsh uplands, and the rapid increase northward through Lancashire to Morecambe Bay. The local increases shown in Norfolk, the Sussex Weald and the High Peak are probably real features, though they may well be less marked in other years. On the other hand, the local minimum recorded for a small stream (Allt Bhlaraidh) west of Loch Ness appears out of accord with other available records in the region (Beauly, Ness and Lochy) and it is possible that it may be untrustworthy.

It is evident that the run-off (R) may be expected to be less than precipitation (P) in the same area by an amount representing the water lost by evaporation from the ground or transpiration from natural vegetation or crops. The amount of this difference ($P-R$) is thus a measure of evapo-transpiration and may be termed the 'run-off deficit' (D). Values of D in inches are expressed cartographically in Fig. 2. Here the range of variation in the recorded values is quite small (28·2/12·3 = 2·3 only) and, in fact, most of the values depart only by small amounts from 20 in. a year. There is a detectable tendency for higher values to occur in the south, where evaporation can be expected to be greatest, but high values are also recorded in the Scottish Highlands, presumably reflecting the great amount of exposed water available for evaporation. Elsewhere the variations appear a little capricious, and doubtless reflect in some way the influence of particular weather spells in certain areas. This map will probably show much variation

from year to year in the location of the isopleths; but the broad fact that it reveals—namely, that evapo-transpiration levies a sort of overhead charge of roughly 20 in. a year from each and all the river basins of Britain—is doubtless a long-term reality. Figs. 1 and 2 are, in fact, complementary. Together they account for the whole of the rainfall received in the water year ($R + D = P$), but they show that the geographical variation of the fractions disposed of by run-off and by evapo-transpiration is radically different. It is to be doubted whether there has previously been any general appreciation of this difference by water engineers or others.

The third map (Fig. 3) shows variations tabulated in the report as "gross mean discharge per square mile", that is, the mean quantity of water in cubic feet contributed every second from every square mile of the catchment basin concerned to its total delivery. Since it represents the flow contributed per unit area it would seem appropriate that this quantity should be called the 'specific discharge' (S). Physically it has the same dimensions as the run-off, the two quantities being numerically related thus:

$$\frac{R}{12} = S \times \frac{365 \times 24 \times 60 \times 60}{5280 \times 5280} \text{ or } \frac{R}{S} = 13{\cdot}57$$

Ideally, therefore, the 2-in. isopleth in Fig. 3 should correspond to an isopleth of 27·15 in. of run-off in Fig. 1; but because the nearest isopleths in Fig. 1 are drawn at 20 and 30 in. some divergences, of course, actually appear. The map of specific discharge yields no distributional information not implicit in Fig. 1 but gives numerical expression to a very different way of regarding the same data. Whereas Fig. 1 obviously invites comparison with the rainfall map, Fig. 3 allows one to say simply by inspection that the mean flow in 1955–56 from 120 square miles of catchment in Caermarthenshire probably exceeded 480 cusecs, while the flow from an equivalent area of east Suffolk was probably less than 60 cusecs, though there were no gauging stations operating in either area during the year.

All three quantities so far discussed may show considerable variations from one year to another at a given locality. The quantity mapped in Fig. 4, however, is more likely to be conservative and to reveal essential and persistent differences between one part of Britain and another. This quantity has for twenty years or more been discussed by French geographers under the name *coefficient d'écoulement*, for which it is suggested that an appropriate English term would be 'discharge ratio'. It is simply the ratio R/P expressed as a percentage. When mapped it shows a wide variation ($75/12{\cdot}7 = 5{\cdot}9$) which expresses the combined effects of two fundamental geographical contrasts—that between upland and lowland, and that between the windward and leeward sides of the country. This is really the basic map of the hydrological characteristics of the country, and it is to be hoped that in future gauging stations will be established on the streams of Caithness, the west of Scotland, north-west and south-west Wales, Cornwall, Dorset, East Anglia, Lincolnshire and the north-east of England, to permit the blank areas of the map to be filled in.

When this has been done and mean values of the discharge ratio have been established for the whole of Britain over a period of years, we shall be possessed of a map which will reveal the very different endowment of the different parts of the country in respect of one of its basic resources—available surface water. Prof. W. G. V. Balchin has more than once in recent years stressed that over much of England the increasing demands for domestic and industrial water cannot long continue to be met locally, and has called for a stocktaking of our water resources as a first step to overall planning of water distribution and use[1]. It is urged here that maps of the kind now offered for the first time for Great Britain are basic documents for understanding our water situation and for planning for the future. It is very much to be hoped that the Surface Water Survey will itself, in future annual reports, undertake the presentation of its data year by year in this form, and in due time will undertake the preparation of maps of long-period monthly and annual means.

[1] Balchin, W. G. V., *Geography*, **42**, 149 (1957); *Water and Water Engineering*, **61**, 289 (1957).

THE McGILL–MONTREAL GENERAL HOSPITAL RESEARCH INSTITUTE

By Prof. J. H. QUASTEL, F.R.S.

THE McGill–Montreal General Hospital Research Institute, which has just celebrated the tenth anniversary of its foundation, is housed in an old three-story residence located on University Street, which is in the heart of Montreal, close by the McGill University buildings. It is situated very near the McGill Medical School, the Royal Victoria Hospital and the Montreal Neurological Institute.

The Institute arose as a result of a decision made in 1947 of the Board of Management of the Montreal General Hospital, upon the recommendation of its Medical Board, that the establishment of a laboratory devoted to the solution of medical problems by fundamental biochemical methods would be an important step for the development of medicine in Canada. The primary movers for the establishment of such an Institute were Dr. I. M. Rabinowitch, Dr. C. C. Birchard, Dr. B. S. Johnston and others, all members of the Medical Board of the Montreal General Hospital, who were convinced that medical progress to-day is greatly dependent on biochemical advances and achievements. When the Institute was inaugurated in 1948 it was the first of its kind to be established in a Canadian hospital.

Almost eight years after its inception, when the initial staff of five had grown to thirty, the Institute was incorporated into McGill University. The premises, which had been acquired by the Hospital from the University with funds given by Mr. T. H. P. Molson and the late H. W. Molson, reverted to McGill ownership. A special committee appointed by the Hospital considered that the scope of the Institute's activities would be broadened through a closer association with related McGill departments and McGill teaching hospitals. The incorporation was a natural consequence of the Institute's funda-

mental research work, which remains, however, intimately connected with practical medical problems.

The present somewhat ponderous name of the Institute recognizes a double loyalty, to the Hospital which brought the Institute into being, and with which a close association is maintained, and to McGill University, which embraces the Institute as part of its family of research units. As a member of the McGill Research 'family' the Institute has become a valuable training ground for students and for postgraduate investigators. The present writer is director of the Institute and professor of biochemistry in McGill University; two members of the staff of the Institute, Dr. P. G. Scholefield and Dr. E. H. Creaser, are assistant professors of biochemistry in the University.

The Institute has, at present, a staff of thirty-five, of whom sixteen are students working in the field of biochemistry for their Ph.D. degrees under the supervision of senior members of the Institute, and twelve are post-doctoral investigators. Both the students and post-doctoral investigators are drawn from various parts of the world. At present, as many as twelve different nationalities are represented. There are members, for example, from Canada, Britain, Australia, India, Pakistan, Japan, the Philippines, Hungary, Greece and Poland.

More than 150 original scientific articles have been published, from the Institute, by members of the staff since the Institute was opened about ten years ago. They are all in the biochemical field, and are concerned with investigations mostly undertaken because of their relation to medical problems. Some of the work lies in the cancer field, some in a field of study devoted to problems of the central nervous system, some in the fields of virology and microbial chemistry, and some of the work is associated with the subject of intestinal absorption. The problems that have been, and are being, investigated are concerned with the biochemical behaviour of cancer cells and of embryonic cells, with the effects of antimetabolites on cell processes, with the mode of action of narcotics, anæsthetics, alcohols, and other substances affecting the behaviour of the nervous system, with the metabolic problems concerned with virus growth, with the mode of action of antibiotics, with the role of amino-sugars in metabolism, etc. These investigations, pursued at a fundamental level, make it possible for students in the Institute to acquire a broad experience of biochemical problems and techniques. Much of the work is necessarily enzymological in character, and a good knowledge of the biochemistry of enzymes is indispensable for the approach taken, in the Institute, towards its various problems. Radioactive techniques and procedures are followed in almost every phase of the work. Problems of nucleic acid metabolism and nucleotide synthesis, protein synthesis, phospholipid synthesis, all problems which are being actively investigated in the Institute, require their due quotas of carbon-14, phosphorus-32 and sulphur-35. Geiger counters operate on each floor of the old residence, and precautions have to be taken that no contamination by radioactive materials makes its appearance in the laboratories. Tumour transplantation in animals is carried out fairly extensively, as may be expected in an Institute which has to do with cancer problems, but the fact that transplantation of certain tumours into embryonated eggs is a successful procedure relieves to some extent the pressure on the animal house and the high cost of animal upkeep.

The Institute, now an active biochemical research centre, is very crowded, and there is no part of the old residence, in which the Institute is housed, that is not put to good use. It is well equipped, and it is surprising how well the many rooms of various dimensions serve as laboratories. Much of the laboratory furniture is home-made, and there is an excellent workshop that is indispensable for repair work as well as for the building of instruments.

Almost the entire work of the Institute is financed by grants and fellowships from a variety of organizations such as the National Cancer Institute of Canada, the Cancer Research Society, Inc., the National Research Council of Canada, the Rockefeller Foundation, the National Science Foundation and other scientific societies without the financial support of which the Institute could not survive. A number of commercial firms have also generously assisted the Institute; to these the Institute is very greatly indebted. The fact that the research work of the Institute depends so greatly on the financial help of many organizations, who support its work after due examination and appraisal of submitted projects, makes the task of organizing long-term research programmes a difficult one. It is greatly hoped that the Institute will one day be given a permanent endowment that will make it possible for the Institute to carry on part of its work without financial anxiety.

The Institute has been fortunate in the co-operation afforded it by the various departments of McGill University and its teaching hospitals, and also in the warm friendliness and active help of the chairman of the Biochemistry Department, Prof. D. L. Thomson. As Dr. F. C. James, principal of McGill University, and Mr. W. W. Ogilvie, president of the Montreal General Hospital, have justly stated, in a foreword to a brochure recently issued concerning the Institute, McGill University has long pioneered in many important fields of research. Since the days of Rutherford and Osler, McGill investigators, and others connected with the University, have contributed greatly to scientific and medical knowledge. The Institute is doing its best to maintain this tradition. Its success so far is due largely to the enthusiasm, devotion and hard work of its members, and it looks forward to a very productive future.

OBITUARIES

Dr. G. M. Bennett, C.B., F.R.S.

George Macdonald Bennett was born on October 25, 1892. His father, the Rev. J. E. Bennett, a great admirer of George Macdonald, the Scottish writer, had entered the Baptist ministry but established a private boarding school, Clacton College, towards the end of the past century, putting into practice many ideas which were then unorthodox but are now more generally accepted. Here Bennett received his early education; after the founder's death, the school was continued by Harold Picton, one of Ramsay's brilliant young men who had become associated with it in 1900. It is a tribute to this school, and perhaps more to the young Bennett's

remarkable talents, that when he left it for East London (now Queen Mary) College in 1909 he embarked on an honours course in chemistry which he pursued by day while continuing with a correspondence course for an arts degree in the evenings and at week-ends. The resulting B.A. (1911) and B.Sc. (first-class honours, 1912) by the age of twenty foreshadowed the brilliance of his career.

In 1913 Bennett won an exhibition at St. John's College, Cambridge where he read chemistry, physics and mineralogy, taking a first class in both parts of the Tripos and being elected a Fellow of the College in 1917. He was then working under Prof. W. J. Pope, but his active mind ranged beyond the immediate war-time work, such as that on ββ′-dichlorodiethyl sulphide, and turned to crystallography, which he had learned under Hutchinson, and stereoisomerism.

Soon after the end of the First World War, Bennett worked for a short time with Strange and Graham, a firm of consulting chemists, and then was appointed a demonstrator at Guy's Hospital, London. From here, in 1924, he went as lecturer to the University of Sheffield, where in 1931 he succeeded Prof. W. Palmer Wynne as Firth professor. After seven years he returned to London to fill the vacancy caused by the retirement of Prof. Samuel Smiles at King's College, London, and soon had to cope with evacuation to Bristol. Here, although his department suffered from bombing, Bennett kept the teaching going and maintained an output of research.

In 1945, on the death of Sir John Fox, Bennett was appointed Government chemist. To some, this seemed a strange transition, but those who knew his wide knowledge and his mastery of detail were sure that he would justify the appointment—as he did, for the normal tenure was extended, but he did not live to complete the additional two years.

Space permits only a brief mention of a few of the lines along which Bennett worked, but these are selected to show his wide interests: surface tension and the constitution of liquids; isomerism of some ferrocyanides; reactivity of the chlorine atom in chloro-substituted sulphides; velocities of reactions of various types, particularly with reference to polar effects; glycols and thioglycols; stereoisomerism of disulphides, dioxides and related substances; valency angle of oxygen and of sulphur; crystal form of anhydrous citric acid; configuration of heterocyclic compounds; formation of large-ring sulphur compounds; liquid crystals; mechanism of nitration.

Bennett received the degrees of Ph.D. of London and M.A. and Sc.D. of Cambridge. He was elected to the Royal Society in 1947 and was appointed a Companion of the Bath in 1948. He was among the first old students to be made a Fellow of Queen Mary College. He was an honorary secretary of the Chemical Society from 1939 until 1946, having served on the Council during 1929–32, and was vice-president from 1948 until 1951. He served the Royal Institute of Chemistry on the Council for two years, as examiner for five years, and as vice-president for two years.

In 1918 Bennett married Doris Laycock, a Cambridge graduate, and her tragic death at Christmas 1957 from a rapid form of cancer no doubt aggravated the heart trouble from which he died suddenly and peacefully on February 9, 1959. He combined great gifts with humility and kindliness.

A. D. Mitchell

Dr. H. D. K. Drew

Harry Dugald Keith Drew died in London at the end of December at the age of seventy-two. He was educated at Queen Elizabeth's School, Barnet, and at Birkbeck College, London, graduating B.Sc. in 1910. His active professional career as a chemist began in 1919 when he joined G. T. Morgan, then professor of chemistry in Birmingham, as research assistant, after war service in the R.N.A.S. In 1922 he was appointed to the teaching staff of the University of Birmingham as lecturer in chemistry; in 1930 he became reader in organic chemistry in the University of London at Queen Mary College, a post which he held until he retired in 1947.

Drew's earliest published work was in collaboration with G. Senter and with A. McKenzie, and was concerned with the investigations on the Walden inversion which were then being carried out at Birkbeck College. In his later work, the interest in stereochemistry was maintained and developed along independent lines. The most striking of these researches was a re-investigation of Vernon's observations on the isomerism of the dialkyl telluronium dihalides, which were assumed to be *cis-* and *trans-*isomers resulting from a planar distribution of the valencies of tellurium. Drew established that the difference between the red α-dimethyl telluronium diiodide and the green β-compound is not one of *cis–trans* isomerism; the green compound has a salt-like character, Me_2TeI, $MeTeI_3$, whereas the red α-compound is Me_2TeI_2. He also inferred a tetrahedral distribution of the tellurium valencies. There were other investigations on tellurium and selenium organo-metal compounds, notable among these being the study of the interaction of tellurium tetrachloride with β-diketones.

In a series of papers from 1930 onwards, some in collaboration with the late Prof. W. Wardlaw and his school, the structure of platinum co-ordination compounds was examined in some detail and many of the inconsistencies and earlier conclusions corrected. Other topics which attracted Drew's interest were chemiluminescence and the metal lakes formed from orthohydroxy azo-compounds. While he was still on the staff in Birmingham, Drew was drawn into work with W. N. Haworth on the investigation of the ring structures of the sugars, and in this both he and E. L. Hirst played an important part in this revision of the then accepted structures.

In the late 1920's, Drew spent a period in Pregl's laboratory in Graz, and he returned enthusiastically in favour of the new system of micro-analysis of carbon compounds. He set up a laboratory for teaching Pregl's methods, and gave regular courses of instruction both in Birmingham and in London to undergraduate and graduate students. He also set up what was probably the first laboratory for the routine microanalysis of carbon compounds.

Drew was a man of many gifts and interests, among them an active interest in tennis and cricket, yet he never conquered his shyness and reticence to become well known even to his colleagues. The over-riding interest in his life was the practice of chemistry, and to those who had the opportunity of seeing him work at the bench, his skill with small amounts of material and his ability to extract pure crystalline products from the most unpromising material seemed uncanny. He was a man who practised his craft essentially for the satisfaction of accomplishment and not for any personal gain or reward. W. J. Hickinbottom

NEWS and VIEWS

Royal Society of Edinburgh: New Fellows

At the ordinary meeting of the Royal Society of Edinburgh, held on March 3, the following were elected Fellows of the Society: Dr. S. Alstead, regius professor of materia medica, University of Glasgow; Dr. H. Barnes, principal scientific officer, Marine Biological Station, Millport; Dr. D. Borwein, lecturer in mathematics, University of St. Andrews; Dr. A. F. Brown, lecturer in natural philosophy, University of Edinburgh; Prof. R. Brown, professor of botany, University of Edinburgh; Dr. H. E. Butler, principal scientific officer, Royal Observatory, Edinburgh; Prof. R. Cruickshank, professor of bacteriology, University of Edinburgh; Prof. J. Drever, professor of psychology, University of Edinburgh; Mr. W. D. D. Fenton, chairman, Uganda Electricity Board; Prof. J. C. Gunn, Cargill professor of natural philosophy, University of Glasgow; Prof. A. A. Harper, professor of physiology, King's College, Newcastle upon Tyne; Prof. A. Macdonald, professor of bacteriology, University of Aberdeen; Dr. W. S. Mackenzie, lecturer in geology, University of Manchester; Prof. R. H. Matthew, professor of architecture, University of Edinburgh; Dr. T. A. Munro, physician-superintendent, Royal Edinburgh Hospital for Mental and Nervous Disorders; Dr. E. M. Patterson, lecturer in mathematics, University of Leeds; Prof. W. L. M. Perry, professor of materia medica, University of Edinburgh; Dr. D. L. Pursey, lecturer in mathematical physics, University of Edinburgh; Dr. J. H. Sang, assistant director, Agricultural Research Council Poultry Research Centre, Edinburgh; Dr. R. J. Scothorne, senior lecturer in anatomy, University of Glasgow; Dr. M. A. H. Tincker, principal, North of Scotland College of Agriculture, Aberdeen; Dr. D. Traill, research director of I.C.I., Ltd. (Nobel Division), and director of research; Prof. A. D. Walsh, Baxter professor of chemistry, Queen's College, Dundee; Dr. E. W. Walsh, senior lecturer in physiology, University of Edinburgh; Mr. K. Williamson, migration research officer, British Trust for Ornithology, Oxford.

Chemical Engineering at Cambridge: Prof. T. R. C. Fox

Many will learn with surprise and dismay that Prof. T. R. C. Fox has decided to relinquish the Shell chair of chemical engineering in the University of Cambridge, due to ill-health. When the chair was established in 1946 the number of university departments in chemical engineering in Britain was woefully small and the electors for the professorship had some difficulty in finding the right man for a position that would unquestionably have a great influence on the teaching of chemical engineering in Britain. Prof. Fox had taken a keen interest in the work of this Department from the first mention of its setting up by the Shell Company, and with his background of four years in Imperial Chemical Industries, Ltd., at Billingham, followed by a period as a lecturer in mechanical engineering at Cambridge, Prof. Fox, at the early age of thirty-four, was an outstanding choice. He was already well established at Cambridge, having been an undergraduate at Jesus and a Fellow of King's, and the past twelve years have shown how well this choice has worked out. The Department has built up a reputation in chemical engineering throughout the Western world, and several chairs of chemical engineering in British universities are now occupied by men who have served with Prof. Fox at Cambridge. All those who know him will trust that his health will soon be fully restored.

Prof. P. V. Danckwerts, G.C., M.B.E.

Prof. P. V. Danckwerts was one of the first of those to take part in the building up of the Shell Department of Chemical Engineering at Cambridge, and it does not detract from the feeling of loss that Cambridge will experience in losing Prof. Fox to say that it is a very pleasant thought that the chair will be occupied by Prof. Danckwerts, who is forty-two. His scientific education was begun at Oxford, and after war service in the R.N.V.R., during which he was awarded the George Cross, he spent some time at the Massachusetts Institute of Technology. He returned from there in 1948, in order to take up a position at Cambridge in the new Department, and later joined the U.K. Atomic Energy Authority as deputy director of research and development in the Industrial Group. In 1956 he was invited to take up a professorship in the Department of Chemical Engineering at the Imperial College of Science and Technology, London. During his stay at the Imperial College he has been actively concerned with the re-organization of the syllabus for the teaching of chemical engineering in the University of London and he will bring much experience, both in modern industry and in the teaching of chemical engineering, to Cambridge.

Department of Anthropology, Government of India: N. K. Bose

Mr. Nirmal Kumar Bose, reader in anthropogeography in the University of Calcutta, has been appointed director of the Anthropological Department, Government of India. He took his B.Sc. in geology and his M.Sc. in anthropology in the University of Calcutta. He is well known for his work on the dating of Indian architecture, where documentary evidence is seldom available, and there has been an unfortunate tendency to base dates on a highly hypothetical history of Indian æsthetics. He has done much to introduce more objective methods. He has discovered several sites with palæolithic artefacts. He has worked, and directed the work of others, among tribal peoples. These peoples number about twenty-five millions, and he and his pupils have worked not only on their cultural anthropology but also on their demography. While a few tribal communities have been intensively studied, no comprehensive survey of this vast population exists, and Mr. Bose is keenly aware of the challenge which they offer to a State which has abjured imperialistic methods.

Mr. Bose has also worked on the cultural anthropology of more civilized sections of the Indian people, including certain of their festivals, and on the social

changes which are now occurring in rural Bengal. Some of this work is available to readers of English in his book, "Cultural Anthropology", and in the pages of *Man in India*, of which he is an editor, but much of it has been published in Bengali. Like the English scientists of the seventeenth century, Indian scientists are now faced with the dilemma of publishing in an international language or attempting to educate their own countrymen. Mr. Bose, with his emphatic belief that anthropology begins at home, has often chosen the latter alternative, and for this reason readers of English may under-estimate his work. Mr. Bose has been a successful and much-loved teacher, and may therefore hope to succeed in his intention to establish a working relation between the Department and the universities.

Artificial Planet 2

The United States *Pioneer* 4 space vehicle, launched from Cape Canaveral in Florida at 05.10 hr. U.T. on March 3, travelled past the Moon to become the second artificial planet of the Sun. The launching missile had four stages of propulsion : the first stage was the United States Army *Juno* 2 rocket, and the later stages were made up of clusters of solid-fuel rockets. The vehicle, conical in shape and with a mass of 13 lb., carried instruments to measure the intensity of the corpuscular radiation in the vicinity of the Earth, and a photo-electric sensor which, if the vehicle passed close enough, was to register light from the Moon. A radio transmitter with a frequency of 960 Mc./s. was also carried, with batteries to last for four days. By means of these signals the vehicle was successfully tracked by the Jodrell Bank radio telescope to a distance well beyond the Moon.

The vehicle, which attained an initial speed of 6·91 miles per second, passed the Moon at a distance of about 37,000 miles at 22.24 hr. U.T. on March 4, some 41 hr. after it was launched. It then flew on into an orbit around the Sun, and its distance from the Sun is expected to vary between 91·7 and 102 million miles. Its perihelion distance is, like that of Artificial Planet 1 (see *Nature*, **183**, 83; 1959), almost the same as that of the Earth, and the orbital plane is inclined at only a very small angle to the ecliptic. The orbital period about the Sun is expected to be 392 days, with the first perihelion on March 17.

New Laboratory for Research on Plutonium

The Battelle Memorial Institute is to erect a new laboratory designed especially for studies of plutonium at its Nuclear Research Center outside Columbus, Ohio. It is hoped that the laboratory will be in operation by midsummer. It will be particularly well adapted to the study of plutonium as a reactor fuel material. This is a natural extension of the Institute's work in reactor and fuel element metallurgy, which dates back to 1942. The laboratory will be used by both governmental and industrial groups. Research at present planned for the laboratory will focus on alloys and compounds of plutonium, as well as plutonium itself. The new one-story building will provide 1,440 sq. ft. of space and will contain a variety of conventional and specialized equipment for the development of plutonium fuel elements. The research reactor, hot cells and critical assembly laboratory in operation at Battelle's Nuclear Center will provide supporting services and facilities for workers in the new plutonium laboratory.

Cyanamid European Research Institute, Geneva

Cyanamid, one of the leading chemical and pharmaceutical manufacturers of the United States, has recently completed plans for setting up a basic research laboratory, to be known as the Cyanamid European Research Institute, Inc., to be situated in Geneva. The new scientific centre, which is to employ British, French, German, Swiss and other European scientists, will be solely devoted to long-range research in the chemical and biological sciences. The Institute has acquired an 8½-acre tract of land in the Cologny section overlooking Lake Geneva. This property includes a large residence which will be converted and extended for use as laboratories.

Production and Marketing of Radioactive Isotopes in Britain

To meet the increasing demand for radioactive isotopes throughout the world, the U.K. Atomic Energy Authority has re-organized the production and marketing of isotopes, which has hitherto been shared between the Radiochemical Centre at Amersham and the Isotope Division at Harwell. It has been decided to widen the scope of the Radiochemical Centre, under the direction of Dr. W. P. Grove, to form a single comprehensive organization for producing and marketing all such isotopes. The Radiochemical Centre has its headquarters and principal laboratories at Amersham and will have irradiation facilities at Harwell and at other sites of the U.K. Atomic Energy Authority.

The re-organization is already effective, but users of radioisotopes should continue, for the time being, to order their requirements from Amersham or Harwell. Research into the properties of isotopes and new applications of them and their radiations will be continued at the Isotope Research Division, Harwell, and at the Wantage Radiation Laboratories. This Division will continue to operate the Isotope School; both the Radiochemical Centre and the Isotope Research Division will remain part of the Research Group of the Atomic Energy Authority.

Agricultural Aviation

The use of aircraft in agriculture and forestry is by no means new and has made especially outstanding contributions to food output in newly developed areas. The aeroplane has also had some influence on traditional farming methods, and there is no doubt that the use of aircraft in farming will increase in the future. It is therefore appropriate that a new periodical, *Agricultural Aviation* (1, No. 1. Pp. 23. Published quarterly. Subscription rates per annum : Europe, 24*s*., 1,500 French francs ; United States and Canada, 3.50 dollars. The Hague : E.A.V. v.d. Boschstraat 4, 1959), should be entirely devoted to this topic. It is published by the European Agricultural Aviation Centre at The Hague, but the contents are by no means limited to agricultural aviation in Europe. On the contrary, it should serve as a source of up-to-date information on a world-wide scale, and for this reason it is published in two editions, in English and French, respectively. The first issue contains two papers from member countries. One, by G. H. Brenchley, of the British National Agricultural Advisory Service, gives an account of trials carried out over the past two years in the control of potato blight by aerial spraying. The second, by G. Schumacher (Germany), concerns

the control of leaf cast in common pine. There are also descriptions of new types of agricultural aircraft and equipment and extracts from recent agricultural aviation literature.

Selborne Society Library

THE Selborne Society has deposited its library, which was started in 1895, in the care of the Ealing Public Libraries, and thus made it available to all. The catalogue (pp. 34. Ealing: Central Library, 1958) has been compiled by the staff of the Ealing Reference Library and is arranged in six sections: manuscripts; editions of the "Natural History of Selborne"; other works by Gilbert White; works on Gilbert White and Selborne; books on natural history in general; and other books. It is hoped that the collection, already supplemented by the larger stock of Ealing Public Libraries, will be further augmented by additions from the Society and the public.

Transvaal Museum, Pretoria

THIS well-known Museum, in its annual report for the year ending March 31, 1958 (pp. 48. Pretoria: Transvaal Museum, 1958), records progress in its educational and scientific activities. Lack of space, though a familiar complaint, is now a very serious matter and constitutes a grave hindrance to the efficient functioning of the Museum. Several field trips have been undertaken during the year and in consequence much valuable material has accrued to the collections. The staff have been active in research and publication and continued to give freely of their time in lectures, talks and demonstrations to local cultural organizations. Temporary exhibitions were re-instituted during the year and placed on display each month in the entrance hall. Objects given to President Kruger, but not actually used by him, were transferred from the President's Residence and displayed in cases.

"Flora Europaea"

IN a short publication, Dr. V. H. Heywood has set out basic ideas and information relating to a projected new European Flora ("The Presentation of Taxonomic Information: A Short Guide for Contributors to Flora Europaea". Leicester University Press, 1958). In a foreword, Prof. T. G. Tutin, who is chairman of the Organizing and Editorial Committee, has explained that the main aim of "Flora Europaea" is to consolidate and correlate previous work. This comprises the studies and compilations of more than two centuries and involves contributions from some 20–30 countries. It is hoped to produce a well-balanced, critical survey, in which all relevant information concerning angiosperms, gymnosperms and pteridophytes will be assimilated and presented within a uniform framework. The Flora is intended to be of broad usefulness, not only for taxonomists, but also for other professional botanists, agronomists, foresters, and so on. It is expected that it will be completed within a period of about 12–15 years and that it will comprise three or four volumes. In the pamphlet under consideration, full information is given regarding standard procedures to be used in the preparation of the Flora. The sponsors are the Linnean Society of London, and the secretary of the Organizing and Editorial Committee is Dr. V. H. Heywood, curator of the Herbarium, University of Liverpool.

The Indian National Scientific Document Centre

THE demands on the services provided by the Indian National Scientific Document Centre, for which the Council of Scientific and Industrial Research provided Rs. 4,81,000, compared with Rs. 1,50,000 in 1953–54, increased by 15·2 per cent in 1957–58, and 6,202 out of 6,994 requests were met (Insdoc Report, 1957–58. Pp. ii+22. New Delhi: National Physical Laboratory of India, 1958). These included compilation of 126 bibliographies, 39 technical inquiries and the supply of copies of 5,290 articles, 44·2 per cent coming from Delhi libraries and 15·6 per cent from other Indian libraries. Requests were also received for 305 photocopies of diagrams for research papers, etc., and 441 translations were supplied out of 507 requested. The size of the Insdoc List of Current Scientific Literature has been increased and from January 1958 the *Bibliography of Scientific Publications of South and South East Asia* is being published monthly.

Snowdonia

"SNOWDONIA", issued for the National Parks Commission as National Parks Guide No. 2 (pp. xii+104+17 plates. London: H.M. Stationery Office, 1958. 5*s*. net), was prepared by the Snowdonia Park Joint Advisory Committee under the editorship of E. Vale. It includes descriptions of the geology of the Park by T. C. Miller, its plant life by Prof. P. W. Richards, and its fauna by Prof. F. W. R. Brambell, as well as notes on the principal antiquities within the Park, on mountaineering and on country-going and communications. There is also a full topographical description of the Park. The guide-book is well illustrated, and with a sufficiency of maps, an adequate bibliography, as well as lists of useful addresses, it should fill two important functions: the clarification of public understanding as to the purpose and functions of a national park; and the assistance of those who visit the Park. The National Parks Commission and the Snowdonia Park Joint Advisory Committee are to be congratulated on a first-rate piece of work, admirably designed for its purpose.

Availability of Technical Films used at the Geneva Conference

FORTY-FIVE technical motion pictures first shown last September in Geneva at the Second International Conference on the Peaceful Uses of Atomic Energy are now available for loan and sale from the U.S. Atomic Energy Commission. The 16-mm. films, most of which are in colour, cover major nuclear applications and research activities. They were sponsored by the Atomic Energy Commission, its industrial and university contractors and, in a few cases, by private industrial organizations. Most of the films will be lent on request to industry, advanced educational institutions, research organizations, Government agencies, etc., by the eleven film libraries of the Atomic Energy Commission, each of which serves a specific geographical area within the United States.

All forty-five Geneva films are also available for sale from the following sources: Byron, Inc., 1226 Wisconsin Avenue, N.W., Washington 7, D.C.; Capital Film Laboratories, Inc., 1905 Fairview Avenue, N.E., Washington 2, D.C.; Consolidated Film Industries, 959 Seward Street, Hollywood 38, California. The Washington and field libraries also have about seventy other, less technical, films appro-

priate and available for loan to schools, industry, and other audiences of laymen. Inquiries about the loan and sale of films to foreign users should be sent to the Public Information Service, U.S. Atomic Energy Commission, Washington 25, D.C. All films are available now in English for sale abroad, and will soon also be available in French, Spanish or Russian. An overseas loan programme is being arranged through the United States Information Agency.

Gas Chromatography

A special group has been formed under the auspices of the Analytical Chemistry Section of the International Union of Pure and Applied Chemistry to make recommendations for a standard terminology in gas chromatography. The group consists of: Dr. D. Ambrose (Great Britain) (*chairman*), Dr. A. T. James (Great Britain), Prof. A. I. M. Keulemans (Netherlands), Dr. E. Kovats (Switzerland), Dr. R. Röck (Germany), Dr. C. Rouit (France) and Dr. F. H. Stross (United States). As a basis for their work, the group plans to take the two papers, "Presentation of Gas–Liquid Chromatographic Retention Data", by D. Ambrose, A. I. M. Keulemans and J. H. Purnell (*Analyt. Chem.*, **30**, 1582; 1958), and "Terms and Units in Gas Chromatography", by H. W. Johnson and F. H. Stross (*ibid.*, **30**, 1586; 1958). Comments about these papers or related subjects will be welcomed from those interested, and correspondence can be addressed to Dr. D. Ambrose, National Chemical Laboratory, Teddington, Middlesex, or to any member of the group.

Indian Society of Genetics and Plant Breeding

At the nineteenth annual general meeting of the Indian Society of Genetics and Plant Breeding held on January 23, at New Delhi, the following were elected as office-bearers of the Society for 1959: *President*, Dr. R. H. Richharia; *Vice-Presidents*, Dr. A. B. Joshi, Prof. P. N. Bhaduri; *Secretary*, Dr. M. S. Swaminathan; *Treasurer*, Dr. N. L. Dhawan; *Editor*, Dr. B. P. Pal; *Councillors*, Prof. P. Maheshwari (Northern Zone), Dr. E. K. Janaki Ammal (Mid-Eastern Zone), Dr. S. K. Mukherjee (Eastern Zone), Dr. A. R. Gopal-Ayengar (Central Zone), Dr. T. R. Mehta (Western Zone), Dr. N. R. Bhat (Southern Zone). It was decided at the meeting that henceforth papers on animal genetics and breeding should be included within the scope of the *Indian Journal of Genetics and Plant Breeding*.

Postgraduate Awards in Agricultural Research

The Agricultural Research Council has recently issued a useful booklet giving details of the Research Studentships and Fellowships which the Council is offering in 1959. The booklet also gives information about the openings in the agricultural research and advisory services. Two veterinary research fellowships, tenable for three years, will be open to workers holding a veterinary qualification who have had not less than three years experience in veterinary research, and three junior agricultural research fellowships, also tenable for three years, will be open to honours graduates with not less than three years postgraduate experience. In addition, the Council is again offering up to thirty postgraduate studentships in agricultural research including veterinary training grants, applications for which should reach the Council by March 31. Further information and a copy of the booklet can be obtained, free of charge, from the Secretary, Agricultural Research Council, Cunard Building, 15 Regent Street, London, S.W.1.

Eclipse of the Moon, March 24

There will be a partial eclipse of the Moon on March 24, visible at Greenwich. The circumstances are:

Moon enters penumbra	17h. 56m.
Moonrise at Greenwich	18h. 11m.
Moon enters umbra	19h. 16m.
Mid-eclipse	20h. 11m.
Moon leaves umbra	21h. 07m.
Moon leaves penumbra	22h. 27m.

The greatest fraction of the Moon's apparent diameter obscured by the umbra will be 0·27.

Announcements

Dr. Francis H. Carr, formerly chairman of British Drug Houses, Ltd., has been awarded the Society Medal for 1959 of the Society of Chemical Industry; this Medal is awarded not more than once every two years for conspicuous services to applied chemistry or to the Society.

Lord Hailsham, the Lord President of the Council, is to open the new Warren Spring Laboratory of the Department of Scientific and Industrial Research, at Stevenage, on June 29. Its initial programme will include work on mineral processing, the synthesis of oils and chemicals from carbon monoxide and hydrogen, and research aimed at the suppression of atmospheric pollution. Much of this work will be of a chemical engineering character and will require basic chemical engineering research to be undertaken in parallel with it. For the time being, research on atmospheric pollution will continue at the Atmospheric Pollution Division, Warren Spring Laboratory, River Way, East Greenwich, London, S.E.10.

A conference on Silicon Carbide, sponsored by the U.S. Air Force Cambridge Research Center, will be held at John Hancock Hall, Boston, Mass., on April 2 and 3. Details can be obtained from the chairman, Dr. J. R. O'Connor, Materials Research Unit, Air Force Cambridge Research Center, Bedford, Mass.

The symposium on vaccination against tuberculosis with non-living vaccines, which was to have been held in Florence during April 5–7 (see *Nature*, January 17, p. 154), has been postponed until September. Further information can be obtained from Prof. G. Buonomini, Centro per la Vaccinazione Antitubercolare, Universita di Pisa.

A symposium on Molecular Structure and Spectroscopy will be held at the Department of Physics and Astronomy, Ohio State University, during June 15–19. For further information, or for a copy of the programme when it becomes available, write to Prof. R. A. Oetjen, Department of Physics and Astronomy, Ohio State University, Columbus 10, Ohio.

The annual meeting of the Air Pollution Control Association will be held at the Hotel Statler in Los Angeles, California, during June 22–26. At the technical sessions papers will be presented by outstanding authorities covering the control of air pollution. Proceedings, incorporating copies of all technical papers, will be published.

Erratum. A mistake was made in the manuscript of the communication entitled "Discrepancy between the Distributions of Iodine in Human Serum when estimated by Iodine-131 and Iodine-127" by Drs. S. C. Werner and R. J. Block (*Nature*, February 7, p. 406); in Table 1, col. 2, for "33" read "3".

DARWIN, WALLACE AND LINNÆUS CELEBRATIONS IN SINGAPORE

A CONGRESS was held in Singapore during December 2–9 to celebrate "the Centenary of the formulation of the theory of Evolution by Charles Darwin and Alfred Russel Wallace and the Bicentenary of the publication of the tenth edition of the 'Systema Naturæ' by Linnæus".

It was particularly fitting that this Congress should have been held in Singapore for, although it honoured equally the works of Linnæus, Charles Darwin and Alfred Russel Wallace, it directed special attention to the work of Wallace, who was one of the greatest biologists ever to have worked in south-east Asia. Although it was inspired and run by a small body of organizers without any form of public recognition, and although it was financed solely by response to personal appeals, the Congress achieved international status and standards. Much credit goes to the organizers, the sponsors, and all who participated.

Twenty-three scientists visited Malaya to participate in the Congress, from Britain, Holland, India, Ceylon, Thailand, Sarawak, Hong Kong, Formosa, Australia, Hawaii, Korea and the United States. These joined with Malayan and Singaporean scientists to form a group of some sixty persons who contributed scientific papers, exhibitions, evening discourses and film shows, and attended excursions into primary forest and mangrove swamps.

Nearly six hundred members were enrolled, and attendances at meetings were consistently high. The papers delivered were of high quality and, due to good chairmanship, the meetings kept to the time programme, and adequate time was available for some stimulating discussions.

The Chief Minister of Singapore, Tun Lim Yew Hock, welcomed the visiting scientists and members of the Congress at an inaugural ceremony, which was held at King Edward VII Hall. Prof. J. B. S. Haldane (Calcutta) was then installed as president of the Congress by the vice-chancellor of the University of Malaya, Dr. A. Oppenheim. Prof. Haldane then delivered his presidential address—"The Theory of Natural Selection To-day"—to a large and colourful gathering of members and distinguished guests. The president emphasized the stimuli gained by Linnæus, Darwin and Wallace through working in peripheral areas where lack of knowledge was a challenge. He suggested that the next major biological advance may well come for similar reasons from peripheral places such as Singapore, or Calcutta, where this challenge still remains and where the lack of complex scientific apparatus drives biologists into different and long-neglected fields of research [see p. 710 of this issue of *Nature*].

The first scientific session constituted a general introduction to the Indo-Malayan Region. R. Ho (Malaya) reviewed the geological history and present geographical features of the region; E. J. H. Corner (Britain), official representative of the Royal Society, directed attention to the need for work on the rain forests of Malaysia before it was too late, and illustrated the inadequacy of our present knowledge of the area by a series of fundamental questions that remain unanswered as yet. Tom Harrisson (Sarawak) proceeded to review the changes that have occurred in Sarawak since Wallace's time, some of which were attributable to Wallace himself, such as the regrettable decimation of the orang-utan.

The papers presented in the section on evolution reflected the broad spectrum of modern non-experimental evolutionary studies. The phylogeny of fishes was considered by A. Fraser-Brunner (Singapore), of lamellibranchs by R. D. Purchon (Singapore), and of the agnathan head by R. Strahan (Hong Kong). Problems of comparative anatomy were dealt with by D. D. Davis (Chicago) and D. Barker (Hong Kong). Zoogeography was represented by a paper by J. L. Gressitt (Honolulu). Perhaps most significant was the strong emphasis on the operation of evolutionary mechanisms within small natural populations, representing promising attempts to document from Nature the mathematical models of Fisher and Wright and the laboratory experiments of Dobzhansky and others. Of a total of nine papers, three—by G. S. Carter (England), H. G. Andrewartha (Australia) and W. S. S. Van Benthem Jutting (Holland)—were concerned with one aspect or another of this important problem.

The session on parasitology and entomology opened with a review by A. A. Sandosham (Singapore) of the evolution of the parasitic mode of life. R. Hoeppli (Singapore) gave an entertaining review of the growth of knowledge of tapeworms, illustrating the value of the sadly neglected historical approach. J. R. Audy (Malaya) discussed evolution of parasitism in trombiculid mites; W. W. Macdonald (Malaya) reviewed the distribution and some evolutionary aspects of Malayan mosquitoes with special reference to breeding places, some species being closely associated with man through adoption of man-made breeding places. This made an interesting comparison with the discussion by L. W. Quate (Honolulu) of different patterns of dispersal and of evolution in the islands of Micronesia by two families of Diptera—empids, largely airborne, and psychodids, largely dispersed by man. J. R. Audy, in a second paper, noted that many parasites are habitat-specific rather than host-specific, or depended for transfer on particular features of host-behaviour, and stressed the value of parasites as 'ecological labels' to give ecological information about their hosts. Finally, Kim Hon-Kyu (Korea) described the life-history and host relationships of a wasp parasitic on a moth which is a potential source of silk in Korea.

At the session on zoogeography, Wallace's Line was not regarded as constituting a significant frontier between two distinct faunal areas either by J. L. Gressitt (Honolulu), who considered the insects, or by L. G. Brongersma (Holland), who has studied the reptiles. In both cases transition was noted rather than abrupt change. H. E. McClure (Malaya) discussed the migration of birds in the Far East and indicated the known flight routes over a wide area. In the absence of any programme of ringing of birds, little is known of the distances travelled by individuals.

Of the six papers presented on terrestrial ecology, three were concerned with particular ecological phenomena or particular animal species and the others with the broader point of view usually called 'natural history'. In the animated discussions that followed papers and occurred informally at other times, the most notable feature was a general agreement that the fauna of the tropical rain forest, because of its extreme ecological complexity, is still so poorly understood that it can best be studied from the 'natural history' point of view, for the present leaving precise quantitative studies and intensive testing of ecological principles to workers in simpler environments in other parts of the world.

The first two papers in the session on freshwater ecology, by W. S. S. van Benthem Jutting (Holland) and D. S. Johnson (Singapore), dealt with aspects of the distribution of non-marine molluscs of the Mollucas and of Indo-Pacific freshwater organisms, respectively. The latter paper, which queried the validity of the concept of a separate oriental region, provoked an interesting discussion. A paper on productivity of fishponds and similar bodies of water by G. R. Fish (Malaya) elicited a lively and informative discussion. Other papers included colonization of freshwater habitats by aquatic insects by C. N. Fernando (Ceylon) and the study of breathing behaviour of salamanders and of the climbing perch by H. Spurway (Calcutta).

The genetics section opened with four papers on human polymorphism in South-east Asia. F. Vella (Singapore) described abnormal hæmoglobins in local Chinese, Indians, Malays and others; thalassæmia was not uncommon in Chinese and Malays, sometimes associated with abnormal hæmoglobins. I. Polunin (Singapore) discussed wide variations in blood-group frequencies in different settlements of the same aboriginal tribe, probably due to genetic drift. D. C. Rife (Bangkok) presented dermatoglyphic evidence that Thai people are closely related to Chinese, while E. McEvoy-Bowe (Singapore) described his work on β-amino-*iso*butyric acid excretion in local peoples and gave details of his useful new method for the accurate estimation of urinary amino-acids in chromatograms.

Among later papers, that of C. F. Hickling aroused special interest. He described hybridization experiments with important food-fish of the *Tilapia mossambica* group. Some crosses led to all-male F_1 progeny with marked hybrid vigour, growing about twice as fast as the parent stocks. S. K. Roy (Calcutta) described the wide polymorphism of Indian cattle and buffaloes, with special reference to nipple number. A. G. Searle (Singapore) showed that threshold characters were remarkably common in local wild mice as well as in domesticated animals. He suggested that anencephaly in humans was also due to a threshold mechanism. The last contribution, by Helen Spurway and A. Kumar (Calcutta), on variation under domestication, contained some intriguing suggestions; for example, that "we have not domesticated plants, but they have domesticated us". The chairman (J. B. S. Haldane, Calcutta), in summing up, pointed out the great opportunities in tropical countries for work on human genetics and on cultivated plants and animals in the early stages of domestication.

The section on anthropology covered a wide range of subjects. V. Thambipillai (Singapore) described the physical types of man now living in Malaya, while G. C. Whittow (Singapore) and T. S. Lee (Singapore) both discussed physiological adaptations to life in the humid tropics. I. Polunin (Singapore) concluded that the falling birth-rate in the Muruts of North Borneo may arise chiefly from infectious disease following pregnancy. Tom Harrisson (Sarawak), drawing vividly on his own experiences, gave a stimulating review of the basic problems of living in the jungle. M. Benanzio (Singapore) commented on the high incidence of 'Mongolian spot' in certain populations in Sumatra.

The most interesting contribution in the session on systematics was perhaps the description and discussion by D. Barker (Hong Kong) of the interesting crustacean *Thermosbaena mirabilis*, representative of the small and often neglected order Thermosbaenacea. Further papers were presented by D. S. Johnson (Singapore), P. J. van der Feen (Holland) and L. G. Brongersma (Holland) on a variety of topics ranging from variation in freshwater prawns to the fauna of New Guinea.

E. J. H. Corner (Britain) opened the botanical session and concluded from an attempt to reconstruct the evolution of tropical broad-leaved forest that it was perfected at the beginning of the Cretaceous period before there were, apparently, modern birds and mammals such as now use it. H. B. Gilliland (Singapore) directed attention to the importance of the orchid seedling, with its changes in symmetry, to plant morphology. J. Wyatt-Smith (Malaya) suggested that the vegetation of Pulau Pangkor in the Malacca Straits was destroyed by the eruption of the Toba Lake volcano and that the new flora is of oceanic type, depending mainly on wind- or animal-dispersal of seeds. E. A. Rosenquist (Malaya) discussed the physiology and genetics of palms; G. A. Prowse (Malaya) described new species of Flagellata which provide important sources of fish-food in the fish ponds in which several are characteristic. Yen Yo-Min (Singapore) described the discovery of six *Cercospora* diseases on sugar cane in Formosa. S. K. Roy (Calcutta) gave an account of variation of leaves on the same plant in *Nyctanthes arbor-tristis*. A. Johnson (Singapore) discussed the distribution of Malayan mosses and green seaweeds, an important extension of Malaysian phytogeography. Finally, A. Santiago (Malaya) spoke of the importance of agricultural genetics in applied botany and the shortcomings of reliance on vegetative propagation.

The week-end excursion to Bukit Timah gave a valuable introduction to Malayan rain forest for those to whom it was new, since Bukit Timah is a most important type locality for plants and animals in Malaysia. This is now a carefully protected nature reserve of some 150 acres.

An all-day excursion began with exploration of the mangrove swamp in the Pandan Nature Reserve. The party saw many interesting species, including some large mud-skippers (*Periophthalmus*), one of which was being killed and consumed by the common dog-faced water snake (*Cerberus*).

The scientists visiting Malaya were entertained at a cocktail party at the residence of the chairman of the Organizing Committee on the first evening. On subsequent evenings there was a diversity of public functions, which were particularly appreciated by the many local members who were not free earlier in the day. There were public lectures by J. B. S. Haldane (Calcutta), J. R. Hendrickson (Singapore) and by H. Munro Fox (Britain), the representative to the Congress from the British Association for the Advancement of Science. There were two evenings

of film shows; the first consisted of films taken in Sarawak and presented with a lively running commentary by Tom Harrisson (Sarawak), while the second included films taken in New Guinea and presented personally by L. G. Brongersma (Holland), one taken in North Borneo and presented personally by I. Polunin (Singapore), and one by the Malayan Film Unit, which was introduced by R. D. Purchon (Singapore).

The British Council prepared a photographic exhibition of Darwiniana specially for the Congress, and this was displayed in the Art Museum of the University of Malaya, where it was the object of considerable interest. The exhibition was afterwards displayed in Kuala Lumpur and, so that the maximum benefit should be gained from its preparation, it was then sent on tour; part was sent to Colombo for the meeting of the Ceylon Association for the Advancement of Science and the remainder was sent first to Kuala Lumpur and then to Bangkok. On its return it will be presented to the Department of Zoology, University of Malaya, through the generosity of the British Council.

A bibliographic exhibition was organized by the Foreign Service of the United States and consisted of about three hundred biological publications the majority of which were sent from America specially for the Congress, and the greater part of which has been most generously presented to the library of the University of Malaya. This exhibition was augmented by a smaller number of British works, loaned for the occasion by the Singapore agents of various British publishing houses.

After the Congress, an excursion lasting a fortnight was conducted which traversed the west-coast districts of Malaya as far as Perlis. Special attention was paid to freshwater habitats; the variety observed ranging from rice-fields to torrent-streams, and from acid blackwaters to limestone pools. In addition, visits were made to the Fish Culture Research Station at Batu Berendam, Malacca (*Nature*, **183**, 287; 1959); to the Rubber Research Institute and the Institute for Medical Research at Kuala Lumpur; and to the Fisheries Department and the Bayan Lepas Experimental Farm at Penang. The opportunity was taken to visit and collect from a number of limestone hills and caves.

The post-Congressional field trip to the King George V National Park in the depths of Pahang brought together nine biologists from four continents, whose interests ranged through taxonomy, zoogeography, ecology and evolution. The base of the party was at Kuala Tahan, where they lived in a lodge of the National Park, with adjacent facilities in the Forest Research Laboratory of the Department of Zoology, University of Malaya. The party spent six days walking and collecting through a number of different types of vegetation. They inspected the pattern of quadrats laid out by the Department of Zoology as a part of its long-term programme of ecological research in the jungle. Valuable suggestions were received from the visiting scientists regarding methods of approach and priorities in this programme.

Arrangements were made for some of the visitors to lecture at Kuala Lumpur in the Federation of Malaya, to widen the impact of the Congress. Prof. J. B. S. Haldane gave the substance of his lecture on natural selection and genetics, previously delivered in Singapore, to a special meeting of the Malayan Nature Society. In addition, the Malayan Scientific Association convened a special meeting, at which H. Waring (Australia) discussed the studies, which he had previously presented in Singapore, on the marsupial quokka. H. G. Andrewartha (Australia) described some extremely interesting experiments on mice still in progress in Adelaide. These bear directly on intra-specific elements influencing reproduction and may help to interpret the regulation of population densities. L. G. Brongersma showed and commented on the ciné film of his zoological field work in Dutch New Guinea. The visitors saw the forest reserves and the laboratories of the Institute for Medical Research and of the Rubber Research Institute.

The proceedings of the Congress were covered by the Malayan Film Unit, and it is anticipated that a documentary film will be released in the near future.

Any credit balance remaining in the hands of the chairman of the Organizing Committee will be applied as an endowment to provide a book prize in the University of Malaya as a permanent reminder of this very successful Congress and the events which it honoured. Since the Congress was originally conceived to pay public tribute to the works of Alfred Russel Wallace in Malaysia, it is fitting that this should be known as the 'Wallace Prize'. A few copies of the abstracts of papers and of the programme are available (3*s*. and 2*s*., respectively, including postage).

The scientific papers will be published in full in book form. Applications for the abstracts and programme and advance orders for the scientific papers should be sent to Prof. R. D. Purchon, Department of Zoology, University of Malaya.

R. D. Purchon

THE HAFFKINE INSTITUTE, BOMBAY

DIAMOND JUBILEE

On January 10 the Haffkine Institute in Bombay celebrated sixty years of service in medical research. At the opening ceremony, which was attended by scientists from India and from other countries, the President of the Republic of India, Dr. Rajendra Prasad, said that Dr. W. M. W. Haffkine, founder of the Institute, had built up a tradition which the modern scientific world could best honour by emulation. It might have been a coincidence that a scientist born in Russia and trained in France happened to be in India, when he was assigned the urgent task of preventing plague from taking a heavy toll of lives; but, the President continued, it served to illustrate that scientific advance of all types called for international collaboration. The Bombay Health Minister, welcoming the delegates, announced that the Government of India had given Rs. 300,000 for the expansion of the Institute and that the Government of Bombay had decided to create a special fund for its development.

Waldemar Mordecai Wolff Haffkine was born of Jewish parents at Odessa on March 15, 1860. He

obtained his doctorate in science at the University of Odessa in 1884 and, after working with the physiologist, Moritz Schiff, at Geneva, went to the Pasteur Institute at Paris in 1889 as *préparateur*. Pasteur had introduced vaccine treatment for fowl cholera, and Haffkine in 1892 developed the first successful vaccine against human cholera. Through the influence of Lord Dufferin, British Ambassador at Paris and former Viceroy of India, Haffkine was sent to Calcutta in 1893. The results of his anti-cholera inoculations were so encouraging that the Government of India in October 1896 transferred him to Bombay, where plague had broken out. Haffkine began work at the Petit Laboratory of Grant Medical College; his accommodation consisted of one room and a corridor, and his staff numbered one clerk and three peons, none of whom knew anything of bacteriological methods and had to be trained by him. He succeeded in preparing a prophylactic plague vaccine from pure cultures, which he proved to be harmless on his own person. Its first trial on a plague-stricken community was made in the Bombay House of Correction at Byculla in January 1897. Of 172 untreated prisoners, twelve developed the disease and six died; of 147 inoculated persons, two contracted plague, but none died. During the season at which the plague was prevalent, up to October 1897, 8,142 inhabitants of Bombay applied for inoculation. In April 1897 Haffkine moved his laboratory to a house on Malabar Hill, and in November made another move to premises in Nepean Sea Road, provided by the municipality.

In the following February the Aga Khan placed at his disposal a large house, Khushru Lodge, in Nesbit Lane, Mazagaon. When orders for the prophylactic vaccine began to pour in from all parts of the world, the laboratory became an Imperial concern, and larger premises had to be found at the Old Government House, Parel. The new laboratory was formally opened by the Governor of Bombay, Lord Sandhurst, on August 10, 1899, when Major W. B. Bannerman gave an account of the prophylactic and its action. Three years later Haffkine was appointed director of the Biological Laboratory at Calcutta. He left India in 1916 and lived in retirement at Boulogne-sur-Seine and at Lausanne, where he died on October 26, 1930, aged seventy. A charming, kindly and enthusiastic personality, an accomplished linguist, and a 'bacteriological wizard', Haffkine never married. He was created C.I.E. in 1917.

In 1925 the Government of Bombay decided to call the bacteriological laboratory at Parel 'The Haffkine Institute' to commemorate the name of its founder (*Nature*, **116**, 551; 1925).

To-day, this Institute is the largest research institution of its kind not only in India but also in the East. It has a technical staff of more than one hundred scientists and a subordinate staff of more than five hundred workers, supervized by eight assistant directors and one director, Dr. H. I. Jhala. Its functions are medical research, training of research workers, supply of vital biologicals and diagnostic aids. The vaccine department collaborates with the Plague Committee of the Indian Council of Medical Research in research on plague, and with the World Health Organization in standardization of cholera vaccine. The department of virus diseases acts as a laboratory for an influenza centre in India, in the network of World Health Organization laboratories attached to the World Influenza Centre, London. The Institute is affiliated to the University of Bombay for degrees of M.Sc. and Ph.D. in microbiology, biochemistry, organic chemistry, pharmacology, pathology, bacteriology and zoology. W. R. Bett

UNIVERSITY OF OXFORD TANGANYIKA EXPEDITION

A PARTY from the University of Oxford, with the support of the Government of Tanganyika, made a preliminary scientific survey of the Kungwe-Mahali Mountains on the eastern shore of Lake Tanganyika (longitude 30° E., latitude 6° S.) during July–October 1958.

A herbarium collection was made of the plants of the southern two-thirds of the peninsula by J. G. B. Newbould, T. G. Jefford and B. E. Juniper, of the Botany School, Oxford. This is the first major collection from the area. The material will be assembled and identified at the Royal Botanic Gardens, Kew, for inclusion in the Flora of East Africa. In addition, live orchids were collected and are now in the orchid houses at Kew. Colour photographs were taken of the principal vegetation zones of the area and of many species of flowering plants.

H. F. Lamprey and A. J. Mence, of the Game Department, Tanganyika, and S. Ulfstrand, of the Zoologiska Institution, Lund, made a collection of birds and small mammals. This includes 305 birds, comprising about 135 species. Another 100 species were identified by sight. Among the birds collected were *Campethera taeniolaema* and *Psalidoprocne chalybea*. These records extend considerably the known ranges of these birds. One specimen, a woodpecker of the genus *Campethera*, with affinities to *C. abingoni*, fits no described species and still remains to be identified.

Among the small mammals, which are at present being examined at the British Museum, is the second specimen from Tanganyika of the ground squirrel genus *Protoxerus*.

A survey was also made of the isolated chimpanzee population. When further information is available about the flora, particularly of the forest species, further conclusions may be drawn about the affinities this region has with West Africa. These affinities are already apparent to a certain extent in the records of chimpanzees and *Protoxerus*.

T. E. Stevens completed a geological survey of the south, centre and west of the Mahali Range. Several interesting geomorphological features were observed and a collection of rock specimens was made which will be examined in the Department of Geology, Oxford.

P. L. Simkin, of the University of Oxford, and A. Roggenkämper, of the University of Bonn, made some preliminary anthropological observations among the Waholoholo of the Mahali Mountains. A census was made of the population of some of the villages south of Mount Kungwe. Studies were also made of

social habits and ceremonies, witchcraft and beliefs, with particular reference to the worship of the god Kungwe.

More than 7,000 ft. of 16-mm. ciné film was exposed during the field work of the expedition and on aspects of the village life of the Waholoholo. Songs, musical instruments, drumming, dances and conversation of the Waholoholo, bird song and animal noises were recorded on tape by A. Roggenkämper.

A second expedition to the same area with a different emphasis is being planned for 1959. It will include a zoologist to work on the freshwater fauna and another zoologist, three geologists, one botanist, and probably a medical man and a soil scientist.

B. E. JUNIPER

RADIO TRANSMISSION BY WAVE-GUIDE

THE continually increasing demand for radio frequencies for new and expanding services makes it necessary to review periodically the possibilities of any alternatives to free-space radio circuits. The installation of the trans-Atlantic coaxial cable carrying a large number of telephone circuits has been an outstanding success; and wide-band coaxial cables are in use as alternatives to radio links for conveying television signals over shorter distances. But coaxial cables, using the materials and techniques at present available, are limited to an upper working frequency of about 25 Mc./s., beyond which the attenuation and phase characteristics become unacceptable. With the development in recent years of the technique of generation and reception of ever higher radio-frequencies, corresponding to wave-lengths down to a few millimetres, the hollow tubular wave-guide has become a serious competitor of the coaxial cable. It was therefore very timely that a well-attended convention on "Long-distance Transmission by Wave-guide" was held on January 29 and 30 by the Radio and Telecommunication Section of the Institution of Electrical Engineers.

At the opening session of the convention, Prof. H. E. M. Barlow gave a most interesting and lucid introductory survey of the present technique of guiding radio waves along the outside surface of a single wire and along the inside of a hollow tube. His presentation included demonstrations of the configuration of the electric field both along a wire and inside a tube using a neon gas discharge, of the effect of a dielectric coating on a wire to counteract the radiation from it, and of the manner in which transducers can be arranged to connect cables to wave-guides. One of the great advantages of a copper tubular guide, about 2 in. in diameter, is that its attenuation for circular electric modes decreases with increase of frequency of the radio waves. For example, at a frequency of 40 Gc./s., corresponding to a wave-length of about 7 mm., the attenuation of the guide is about 6 decibels per mile.

At the remaining five sessions of the Convention more than thirty papers were presented; many of these were of a detailed technical nature and they illustrated the advance which is being made in this field in Great Britain and other countries. Some of these papers dealt with both theoretical and practical aspects of avoiding spurious modes of transmission of radio waves in the tube, and the need to discriminate carefully in the conduct of measurements on the characteristics of the guide. Special microwave equipment is being developed to generate the very short waves involved, and particularly to couple the source to the guide, so that waves of the desired mode may be launched with the minimum loss of energy. The last session was devoted to a discussion of the practical possibilities of wave-guides for long-distance transmission, including the economic aspects of such communication systems. The speakers here stressed the fact that not only must such systems have a high degree of stability, but that, so far as possible, they must also be compatible with existing signalling networks as regards facilities for the insertion and extraction of signals at terminals and intermediate points.

On January 31, demonstrations were given of a variety of experiments using millimetre waves associated with tubular wave-guides in the Electrical Engineering Department of University College, London, and at the premises of Standard Telecommunication Laboratories, Ltd., at Watton-at-Stone, near Stevenage.

The text of all papers presented at the convention, together with the associated discussion, will be published in a Supplement to Part *B* of the *Proceedings of the Institution of Electrical Engineers*.

R. L. SMITH-ROSE

HILL FARMING RESEARCH ORGANIZATION

REPORT FOR 1954–58

THE scientific investigation of the problems of hill farming remained largely sporadic and unco-ordinated until it became recognized that this sector of the British agricultural industry is a distinctive form of land-use, based on complex and varying interactions of plant and animal communities which in themselves merit concerted programmes of research to define them more clearly and to attack their major problems. This concept provides the background to the establishment in 1954 of a central research organization and to its objectives and activities; these are clearly and succinctly described in the first report of the Hill Farming Research Organization*.

The extensive distribution of the hill farming areas in Great Britain, and the great ranges in environmental conditions and husbandry systems offer wide scope for study; three factors have tended to restrict,

* Hill Farming Research Organization. First Report, 1954–58. Pp. 88. (Edinburgh: Hill Farming Research Organization, 1958.)

as yet, development of the Organization's work. In the first place, any investigations of such a complex must be on a long-term basis; a small, though full-time, staff can only encompass narrow segments of the field, and in some four years their work can only be preliminary. Secondly, the work must be biased towards 'field' studies, with the niceties and precision of replicated experimentation largely sacrificed. Thirdly, the Organization's three research stations, to the resources of which much of the programme has had to be geared, were inherited from an earlier régime of separate interests in hill farming problems as presented in the areas of the three Scottish agricultural colleges.

At Glensaugh, in Kincardineshire, the basic Blackface sheep stock, on predominantly heather vegetation, is managed according to the custom of the north-eastern counties of Scotland; studies on the dentition and on winter feeding of sheep are in progress, as well as on different breeds and crosses of beef cattle in relation to prolificacy and growth of calves. Lephinmore, in the Cowal peninsula of Argyllshire, provides a varied hill ground in an area of high rainfall, relict from afforestation of plantable land, and thus having peculiar management problems for its Blackface sheep stocks. Sourhope, in Roxburghshire, is the main station for work on Cheviot sheep under conditions reasonably typical of the Cheviot hill areas; investigations on mixed grazing with cattle and sheep had begun in 1951, and others on controlled grazing and on the treatment of cobalt deficiency have since been added.

Animal studies are in two main groups, related respectively to breeding and nutrition. In the former, comparisons of breed and strain are being made with the Blackface and Cheviot breed types, while in respect of the latter, the principal emphasis has been on problems of the nutritional status of hill sheep in winter; various methods and forms of supplementary winter feeding are being examined, responses in the mortality and growth of lambs observed, and differences in feeding habits noted. Particular attention is being given to the plane of nutrition, and methods of 'wintering', of flock replacements during their first winter.

The botanical work is described in more detail. Studies on management involve the effects of burning, drainage, surface seeding and cultivations, sod-seeding, heather grazing, fertilizer treatments, and bracken control. The great significance of the ecological aspects of the hill vegetation influences the investigations on plant communities and their species components and ecotypes; investigations in these fields are being conducted in a wider range of localities and environments beyond those presented in the Organization's own farms. Exploratory studies on the sheep grazing behaviour and preferences in relation to plant communities are being made at Sourhope.

A list of publications is given, and almost by way of appendixes, there are three occasional papers comprising reports on surveys of management systems in Blackface sheep in the north-east of Scotland (with special reference to the incidence of breakdown of incisor teeth with age), and of Border Cheviot sheep, and a short note on the effects of August treatments of a pasture sward on its subsequent yields in autumn, winter and spring.

J. E. Nichols

ULTRA-VIOLET CARCINOGENESIS IN ALBINO AND PIGMENTED MICE RECEIVING FUROCOUMARINS: PSORALEN AND 8-METHOXYPSORALEN

By M. A. PATHAK, Profs. F. DANIELS, jun., C. E. HOPKINS and T. B. FITZPATRICK

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EPIDEMIOLOGICAL evidence clearly implicates solar radiation as a factor in the induction of human skin cancer[1,2]. A factor which appears to protect man from carcinoma induced by exposure to solar radiation is melanin pigment, the darkly pigmented peoples having a markedly reduced incidence of carcinoma of the exposed areas[2–5]. The generalized human albino living in the tropics almost invariably develops squamous and basal cell carcinoma of the exposed surfaces[4]. Similarly, the fair-skinned Caucasians who easily become sunburnt and have a tendency for freckling have a higher incidence of carcinoma of the exposed areas than persons who tan readily[6,7]. The carcinogenicity of ultra-violet irradiation in albino mice has been established by many investigators[3,8–12] and has therefore provided an excellent experimental tool for studying the process of skin carcinogenesis.

Naturally occurring furocoumarins (psoralen, 8-methoxypsoralen or methoxsalen) have recently been used for augmenting pigmentation of human skin following irradiation with long-wave ultra-violet light. This raised the question whether these photoactive compounds might alter the incidence of ultra-violet carcinogenesis. O'Neal and Griffin[13] initiated studies on 8-methoxypsoralen and its effect on ultra-violet carcinogenesis in albino mice. Their initial report indicated that the final incidence of ear tumours induced by ultra-violet irradiation (15·2 to 17·5 × 10^8 ergs/cm.^{2} of short and medium range up to 3200 A.) in mice receiving 8-methoxypsoralen orally (0·5 gm./kgm. diet) was considerably less than that of control mice, evidence suggesting that this photoactive agent had a 'protective' effect against ultra-violet carcinogenesis. The extent of protection afforded by this compound appeared to be proportional to its concentration in diet up to an optimal level of 0·5 gm./kgm. diet. They found, however, in the same experiment that intraperitoneal administration of 8-methoxypsoralen (0·4 mgm./mouse/day)

appeared to increase tumour incidence. Whether the discrepant effects of oral and intraperitoneal administration were related to a difference in the dose or in the route of administration was not resolved.

The present study was undertaken to determine: (*a*) whether 8-methoxypsoralen and psoralen (furo-2',3':6,7-coumarin) when given in oral form protected or otherwise affected the ultra-violet carcinogenesis in albino and pigmented mice; (*b*) if the findings of O'Neal and Griffin[13] could be explained on the basis of differences between the oral and intraperitoneal route of administration; (*c*) the effect of a second furocoumarin, psoralen, as compared to 8-methoxypsoralen (Fowlks *et al.*[14], Pathak and Fitzpatrick[15] and other investigators[16] have reported psoralen to be the most potent photoactive naturally occurring furocoumarin); (*d*) the role of melanin pigment in the skin in ultra-violet carcinogenesis.

Three strains of female mice were used: Swiss strain albino mice, strain *C57BL/6* with black ears, black eyes and hair, and a deep brown strain *C57Br/cd* (Jackson Memorial Laboratory, Bar Harbor, Maine). An ultra-violet irradiation chamber was constructed with two *UA*3 General Electric 'Uviarc' lamps mounted adjacently in aluminium reflectors[13]. The mice were exposed to the total ultra-violet spectrum (mostly short and middle ultra-violet at a distance of 50 cm.). Intensity of illumination under the lamp in a 2 sq. ft. area was determined every 4 weeks by photolysis of uranyl oxalate solutions according to the method of Leighton and Forbes[17]. Quantum yield for the entire spectrum was taken as 0·57 φ. To prevent huddling or movements of mice during irradiation special cages holding each mouse in a separate compartment were used[10,12,13].

Mice 8–10 weeks old with comparable average weight within each strain were randomly divided into cage groups of 20 each. Twenty-eight groups were used: twelve in the albino series, eight in *C57BL/6* strain and eight in *C57Br/cd* strain. Each group received ultra-violet irradiation for six days a week at the rate of $2{\cdot}9 \times 10^4$ ergs/cm.²/sec. Total ultra-violet irradiation received by each group was $14{\cdot}8 \times 10^3$ ergs/cm.² delivered in 850 min.[12]. Irradiation was discontinued after 110 days for albino mice and after 120 days for pigmented mice, following which the observations for tumour incidence were continued for a total of 260 days. Changes in temperature during irradiation were minimized by slow circulation of air from a revolving electric fan. To minimize the possibility of photo-reactivation the animals were housed in a windowless, dark room.

Because the findings of O'Neal and Griffin[13] might be explained by a biphasic response with protection from carcinogenesis by the small doses of 8-methoxypsoralen received in the dietary group, and potentiation by the large doses given in the intraperitoneal group, only oral doses were used in this study. Administration of drugs was carried out by addition of 8-methoxypsoralen or psoralen in a concentration of 0·5 gm. per kgm. of powdered 'Purina Laboratory Chow', which was mixed in a revolving ball mill for 12 hr. Each day's food intake was recorded for each group receiving drugs in the diet. A second method consisted of measured quantities of drug given individually to each mouse by oral feeding from a tuberculin syringe with an attached 18 gauge, semi-curved metal tube 1 in. long. It was possible by slowly inserting the bent tube into the mouth to administer 0·05 ml. suspension of either psoralen or 8-methoxypsoralen prepared in 0·5 per cent gum acacia solution. Wood's light examination of the mice after feeding determined that no spillage of fluorescent compounds had occurred around the mouth. Preliminary tests had indicated that, with oral feeding, the furocoumarins developed their highest concentration in the blood in 1½ hr. Ultra-violet irradiation was therefore given at this time-interval following drug administration. The dose schedule, as shown below, included the range of levels used by O'Neal and Griffin on intraperitoneal dose and also 0·01 mgm., the equivalent of a 20–30 mgm. dose of the drugs in man. Administration of drug was discontinued after 120 days. The experimental schedule is given in Table 1.

Table 1. Experimental Groups and Dose Schedule

Dose	Mouse strains and group numbers		
	Swiss Albino	Brown *C57Br/cd*	Black *C57BL/6*
Controls (no drug)	1, 2	13	21
8-Methoxypsoralen mgm./mouse/day			
Oral—0·01	3	14	22
,, 0·04	4	15	23
,, 0·16	5		
,, 0·64	6	16	24
Dietary 1·7	7	17	25
Psoralen mgm./mouse/day			
Oral—0·01	8	18	26
,, 0·04	9		
,, 0·16	10		
,, 0·64	11	19	27
Dietary 1·7	12	20	28

Each mouse was tagged for individual identification in the observation of effects of irradiation. The mice were examined separately by three observers (M. P., T. B. F. and F. D.) every ten days. The last two observers did not know the identity of the groups until the completion of the experiment. A five-point grading system was used: normal ear, 0; inflammatory response without nodules, 1; suspicious nodules, 2; definite nodule suggestive of cancer, 3; definite tumour, 4. Right and left ear were recorded separately for each mouse. A mouse graded 3 or 4 on either ear by at least two observers was recorded as having a tumour. The analysis is based on the number of mice having tumours and not the total number of tumours. Mice dying after 120 days of irradiation with grades 0, 1 and 2 were considered to have no tumour. The final tumour incidence is expressed as a percentage of the initial number of mice in each group.

Within a week after the beginning of irradiation both the albino and the pigmented mice showed erythema and scaling on the ears. In about three weeks the scale had come loose and ears showed thickening. Both types of pigmented mice showed increased pigmentation of the ears and tail region. This pigmentation was greater in the mice receiving the drugs. Mice receiving 8-methoxypsoralen or psoralen at the 0·64-mgm. level had severe erythema of the ears, nose and face regions. These regions were sufficiently burned to be followed by scar formation, loss of hair, and thickening of the ears. The control animals (groups Nos. 1, 2, 13 and 21) showed less-severe ultra-violet burns. Groups receiving 0·01, 0·04, 0·16 mgm. of 8-methoxypsoralen or psoralen and the dietary groups showed no appreciable damage of irradiated regions. The groups receiving 0·64 mgm. in the pigmented mice showed less damage than the albino groups. During the first 45–100

Table 2. Incidence of Ear Tumour in Three Strains of Mice exposed to Ultra-violet Irradiation after Administration of Furocoumarins (per cent)

Strain	No drug		8-Methoxypsoralen (mgm./mouse/day)					Psoralen (mgm./mouse/day)				
	Controls		Oral administration (mgm.) 0·01	0·04	0·16	0·64	Dietary 1·7 mgm.	Oral administration (mgm.) 0·01	0·04	0·16	0·64	Dietary 1·7 mgm.
Albino mice Swiss strain	60	70	50	45	40	45	65	55	65	40	60	60
Brown pigmented C57Br/cd	15		10	0		0	25	0			5	0
Black pigmented C57BL/6	20		5	5		10	15	0			15	5

Least wholly significant percentage point difference (5 per cent level) = 35 per cent; least wholly significant percentage point difference (1 per cent level) = 40 per cent.

Criterion for comparing any two cage outcomes: P_1–P_2 is significant at $P = 0{\cdot}05$ level if $P_1 - P_2 \geqslant 1/2N + \frac{1{\cdot}96}{\sqrt{N}} \sqrt{P_1 + P_2 - 1/2P_1^2 - P_1P_2 - 1/2P_2^2}$, which reduces, when $N = 20$, to $0{\cdot}025 + 0{\cdot}451 \sqrt{P_1 + P_2 - 1/2P_1^2 - P_1P_2 - 1/2P_2^2}$

days, the observers could not differentiate the control groups from the groups receiving 0·01, 0·04, 0·16 mgm. of drugs. Cataracts developed in many of the animals, in both the control and dietary groups. The pigmented as well as the albino mice developed cataracts. Changes in the eyes were slightly more severe in all the groups on high doses (0·16–0·64 mgm.) of the two drugs. In the albino series, about 5–10 per cent of the mice had tumours of the eyelids. There were no tumours of the eyelid in pigmented groups. The death-rate up to the end of the irradiation period (120 days) was less than 10 per cent in all 28 groups.

The final tumour incidences are summarized in Table 2. In contrast to the findings of O'Neal and Griffin[13], there was no protecting or stimulating effect of 8-methoxypsoralen or psoralen on ultra-violet carcinogenesis in the albino mice. The incidence of tumours in the two pigmented strains of mice was much less than in the albino strain. Five of the groups showed no tumour, four groups had only 5 per cent tumours, two groups had 10 per cent; the rest of the five groups had tumour incidences ranging from 15 to 25 per cent.

The albino mice appeared to develop tumours earlier than the brown or black mice. After starting the ultra-violet irradiation, the control groups in the albino series showed first tumour induction at the end of 90 days; the control groups in both of the pigmented mice strains showed first tumour induction after 166 days. In the albino mice, eight out of the ten groups receiving psoralen or 8-methoxypsoralen, either orally or through the diet, developed tumours after 90–116 days. As compared to albino mice, the rate of tumour induction in both these pigmented mice strains receiving psoralen or 8-methoxypsoralen was very slow. In six pigmented groups, the first tumour induction time was around 147 days. In the rest of the other five groups which showed the development of tumours the induction time was greater than 166 days. The significant variable differentiating the albino and the pigmented strains appears to be melanin pigment. Presence of melanin pigment possibly retards tumour induction, and affords an appreciable protection against ultra-violet carcinogenesis.

There was no effect on the total tumour incidence of different dose-levels of the drug. There was neither potentiation nor protection from ultra-violet carcinogenesis. The albino mice groups receiving the highest dose of psoralen (0·64 mgm.), however, showed a shortened induction time, beginning at only 56 days. This acceleration of cancer induction is not surprising in view of the experimental damage to the animals on this high dose of 0·64 mgm. psoralen. It is of interest that the final tumour incidence did not increase in these animals. As mentioned previously, psoralen has been shown in experiments on humans to have a more potent photoactive effect than 8-methoxypsoralen[15]. This effect of psoralen in the present study was observed in only one albino group receiving the highest dose of 0·64 mgm. It accelerated the rate of tumour induction but not the total incidence. Psoralen and 8-methoxypsoralen otherwise showed similar responses and did not affect the final incidence of ultra-violet carcinogenesis in either albino or pigmented mice.

From these experiments it is concluded that the findings of O'Neal and Griffin[13] indicating that 8-methoxypsoralen provided protection against ultra-violet carcinogenesis are not confirmed. Under our conditions no potentiation of carcinogenesis was demonstrated by 8-methoxypsoralen or psoralen in dose-levels ranging from 0·01 to 0·16 mgm./mouse/day. Dietary feeding of psoralen or 8-methoxypsoralen (0·5 mgm./kgm. diet) did not reveal any protective effect against ultra-violet carcinogenesis. Some factor, possibly the melanin pigment in brown and black pigmented mice, appeared to protect the pigmented mice appreciably against ultra-violet carcinogenesis.

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MUTAGENIC ACTIVITY OF THE ALKALOID HELIOTRINE IN *DROSOPHILA*

By Dr. A. M. CLARK

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NATURALLY occurring chemical mutagens of plants are of considerable general interest because of the possibility that they make an appreciable contribution to the apparent spontaneous mutation-rate, both of the plants in which they occur and of any phytophagous animal species which may be sensitive towards them. In some cases, these mutagens might assume practical importance if they are active following ingestion by agricultural livestock. A number of the pyrollizidine alkaloids from various plants (*Heliotropium*, *Senecio*, *Crotalaria*) have been shown to possess considerable biological activity[1-3]. It therefore seemed worth while to test them for mutagenic properties. This article is intended to direct attention to the mutagenic activity of heliotrine, an alkaloid from *Heliotropium europaeum*[4].

To test the mutagenic activity of heliotrine in *D. melanogaster*, the Muller-5 technique for sex-linked recessive lethals was used. Following an injection of 0·08 μl. of a solution of heliotrine in 0·7 per cent sodium chloride, Canton-*S* males were mated individually to three *Basc* females, fresh females being provided at intervals of 72 hr. Cultures were maintained at 25° C. In the Canton-*S* stock in use in this laboratory, the spontaneous incidence of sex-linked recessive lethals is about 0·1 per cent for sperm produced during the first few days of adult life. All suspected lethals were confirmed in the F_2 and many have been kept in culture for further cytogenetic analysis.

Table 1. PRODUCTION OF SEX-LINKED LETHALS FOLLOWING INJECTION INTO ADULT MALES OF 0·08 μL. OF A 0·3 PER CENT SOLUTION OF HELIOTRINE IN SALINE
Brood interval of 72 hr.

	Brood				
	1	2	3	4	5
Chromosomes tested	558	563	233	116	102
Lethals	31	10	17	6	3
Per cent lethals	5·6	1·8	7·3	5·2	2·9

The existence of perhaps two sensitive periods is suggested by the results in Table 1, representing the distribution of lethals over five successive broods following the injection in the males of 0·3 per cent heliotrine (approximately 0·01 *M*). The relatively small number of chromosomes tested from the last three broods is a reflexion of the partial sterilizing action of heliotrine in *Drosophila*. In fact, if the concentration of heliotrine exceeds about 0·5 per cent, the injection of 0·08 μl. of the solution renders it possible to obtain only the first two broods. The mutagen seems to block the maturation of immature germ cells, so that as soon as the available spermatozoa and spermatids have been utilized, the males are no longer capable of breeding, although they may remain alive and active for as long as three weeks after treatment. Since fertility is not regained within this period, the cell damage caused by the alkaloid is presumably quite irreversible.

If the concentration of heliotrine is in excess of 1 per cent, then only a single brood is obtained, in which the incidence of lethals may be higher than

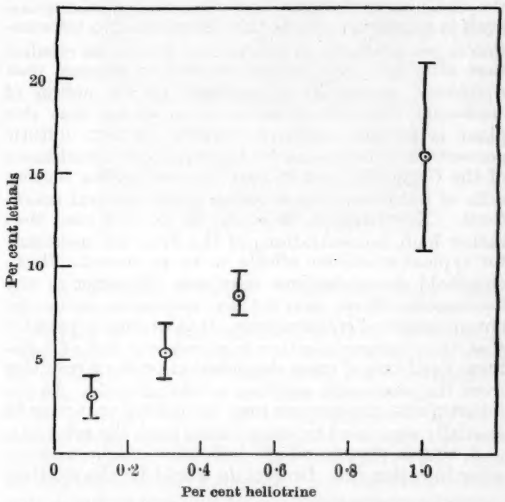

Fig. 1. Percentage of sex-linked recessive lethals (with 95 per cent confidence limits) at different heliotrine concentrations. First brood only

30 per cent. This single brood is often obtained as a result of copulation occurring within 1 hr. of treatment, indicating that the heliotrine does not in itself retard the mating behaviour of the males. Failure to obtain a second brood suggests some degree of destruction of spermatids or, alternatively, an inhibition of spermogenesis. By using alkaloid concentrations of less than 0·5 per cent several broods can be obtained readily, and the mutagenic effect is then found to extend back to pregonial cells. Clustering of lethals is common in these later broods.

Fig. 1 shows the results of an experiment to determine the relation of the dose response for the first brood only (spermatozoa mature at the time of treatment), using a ten-fold range in heliotrine concentration. Under the conditions of test, the relation appears to be linear. At the highest concentration used, however, the sampling error is large owing to the reduced number of offspring that can be obtained. Some deviation from simple linearity might be expected at the higher dose-levels in the light of observations (to be published elsewhere) on the ability of heliotrine to induce large structural rearrangements in *Drosophila*.

Bull, Dick, Keast and Edgar[5] have made an extensive investigation of heliotrope poisoning in sheep, and have shown that consumption of the plant results in severe liver damage. Bull[5] has further shown that heliotrine can produce similar damage to the liver of laboratory rats, while Schoental and Magee[3] have demonstrated the carcinogenic properties of the related alkaloid lasiocarpine.

Crowley and Culvenor[6] have found that different samples of *Heliotropium europaeum* may show considerable variability with respect to alkaloid content; but in none of their assays was there any indication

that the content ever falls to a level at which hepatotoxic effects would not be expected to ensue following extensive feeding on the plant by sheep. However, even if the alkaloid-levels are low or if feeding is relatively restricted, there would now appear to be the possibility that livestock failing to develop toxic symptoms may nevertheless have suffered some degree of genetic deterioration.

The powerful mutagenic activity of heliotrine raises the interesting question of whether *Heliotropium* itself is sensitive towards this chemical. No information is yet available on this point. It may be recalled that although early work[7] seemed to suggest that *Colchicum autumnale* is resistant to the action of colchicine, later investigators have shown that this plant is in fact sensitive towards its own mitotic poison[8,9], and Takenaka[10,11] has reported disturbances of the *C*-mitotic type in root tips and pollen mother cells of *Colchicum* plants living under natural conditions. Nevertheless, it seems to be the case that rather high concentrations of the drug are necessary for typical colchicine effects to be produced. High-threshold concentrations may also characterize any mutagenic effects exerted by heliotrine upon the chromosomes of *Heliotropium*. It is, of course, possible that the mutagenic action is a property not of heliotrine itself but of some degradation product resulting from the enzymatic splitting of the alkaloid. In the intact plant, the enzyme may be lacking or it may be spatially separated by some means from the substrate.

A simple change which heliotrine might undergo after injection into *Drosophila* would be the splitting of the ester linkage, releasing heliotridine and heliotric acid. To test this possibility, hæmolymph and tissue homogenates were tested for esterase activity capable of splitting the alkaloid, but without success. In any event, heliotric acid is only feebly mutagenic when injected into *Drosophila*, while heliotridine is quite inactive, suggesting that the strong mutagenic property of heliotrine itself is probably a property of the molecule as a whole rather than of some degradation product.

My thanks are due to Prof. G. S. Christie of the Pathology Department of this University for first directing my attention to heliotrine as a possible mutagen, and to Dr. C. C. J. Culvenor of the Commonwealth Scientific and Industrial Research Organization, Division of Industrial Chemistry, for providing samples of various pyrollizidine alkaloids.

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COSMIC DUST IN THE ATMOSPHERE

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THE extensive work of Prof. H. Pettersson and his colleagues[1] and the analytical work of Smales *et al.*[2] have established that certain magnetic spherules (about 50μ diameter) obtained from deep-sea sediments are extra-terrestrial. Magnetic spherules, similar in size and appearance to these 'cosmic spherules', have been collected by several observers directly from the air. Buddhue[3] showed that many such spherules could be picked up, daily, by a greased slide. However, vast numbers of these particles appear in chimney fly-ash and some doubt exists concerning the origin of spherules collected, even in isolated places.

During August 1957, a plastic bowl of filtered water, area 1/6 sq. m., was exposed at the top of the light-house on Bardsey Island (North Wales), in the hope of detecting fine dust from the Perseid meteor shower. About fifty black or silvery magnetic balls of around 10μ diameter were collected daily. This number varied according to weather conditions, strong winds and no rain increasing the daily catch considerably. Towards the end of this examination, attention was attracted to certain metallic-looking flakes; and it was established that some of these were metallic iron, copper being immediately deposited from a surrounding bead of copper sulphate solution. X-ray examination of one of these particles showed it to be fine-grained polycrystalline iron.

About a gallon of melt-water, obtained by Mr. L. K. Coachman (Department of Oceanography, University of Washington) from the wall of a crevasse in West Greenland, yielded 19 magnetic spherules ranging in diameter from 5μ to 35μ (mainly about 20μ in diameter). In addition to many black and variicoloured magnetic fragments, four flakes of metallic iron similar to the Bardsey specimens were found. One of these was a remarkably straight needle-shaped object of square-like cross-section 240μ long and 20μ wide.

On occasions during the summer months, aircraft of the Meteorological Research Flight have been collecting samples of dust over southern England at 10,000 ft., while flying at a speed of about 200 m.p.h. A slotted 'Perspex' slide of effective collecting area 10 sq. cm. was thinly coated with gelatine. Each slide, held in an aluminium frame, was exposed from the side of the fuselage, for exactly 30 min. The results of flights carried out on August 11 and 20, 1958, are of particular interest. Three slides were exposed during each flight.

'Terrestrial-looking' sand particles (generally flakes) as large as 150μ were found, but the presence of only a few spherules was surprising. On average, each slide picked up two or three sand grains of about 100μ diameter, a dozen around 50μ and many more in the smaller size-ranges. Only one or two opaque spherules (10μ–20μ) were observed. Among the fragmentary opaque material, which followed a similar size-distribution, several interesting metallic-bearing particles were found.

On a slide exposed during August 20, a large silvery flake (200μ × 100μ × 20μ) was found firmly embedded in the gelatine layer. In parts it was covered with small grey translucent balls which appeared to sprout from the surface, and the particle appeared to be a loosely aggregated structure of small grains. The addition of copper sulphate quickly turned it a matt black-bronze, with here and there bright specks of copper. By softening the gelatine it was possible to lever out a large section, and Fig. 1 shows the impact region on the gelatine, together with a few pieces that remained in position (The tiny specks around the main area are chippings made by a glass fibre.) The extracted section was to be examined by X-rays, but during manipulation in a pool of glue it fell apart. On the same slide another flake, about 50μ in size, embedded like a knife blade in the gelatine, reacted immediately to the copper sulphate test.

The long needle-shaped particle (Fig. 2) is typical of another kind of fragment. This at first did not react to copper sulphate, but later dendritic copper grew out from certain spots which are presumably the sites of cracks in a surface oxide layer. Although most attention was paid to the large fragments, several of the smaller ones deposited copper, particularly after their surfaces had been damaged.

These oxide-coated particles must be similar to those described by Buddhue, who noticed that some of the fragments emitted tiny bubbles when the sample was under acid. He also detected chemically the presence of more iron after the sample had been crushed.

The possible extra-terrestrial nature of these metallic fragments must be seriously considered. On the average, each slide collected about one as large as 100μ, and since sand grains of this size-range occurred with only two or three times this frequency, it seems unlikely that the metallic particles could have been transported from ground-level to 10,000 ft. Industrial dust, collected over Liverpool, has been examined on many occasions, and although metallic iron fragments have been found they are located with the utmost difficulty. These fragments must be abraded from common iron as they are observed to rust quite readily.

The water-bowl technique was again adopted during August 1958. The bowl, of area 1/15 sq. m., was placed on a rocky prominence at the south-west tip of St. Agnes, Isles of Scilly. The winds were mainly in the south-west and since scarcely a day was free from rain the air was particularly clean. A thorough examination of the magnetic fraction in the water samples has now been completed, the non-magnetic portion being preserved for later inspection.

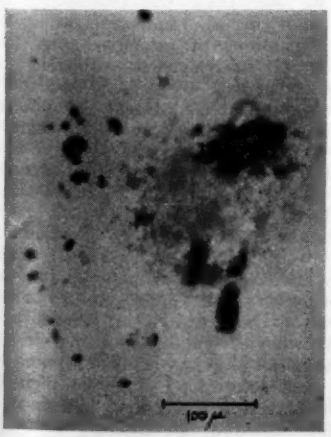

Fig. 1

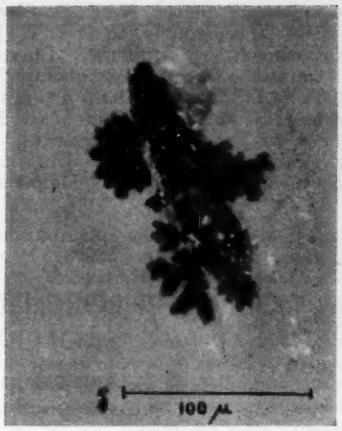

Fig. 2

On average, during a 48-hr. exposure, about a dozen black powdery aggregates varying in size around 40μ were recorded, together with two or three silvery flakes of the same size. For the whole month only 15 spherules about 10μ in diameter were collected; and only three silver flakes and one black flake were found to react to the copper sulphate test either immediately or after slight crushing. But a large (150μ) partly translucent aggregate picked up during the period August 11–13 was observed to deposit copper in a few spots on the surface and between the crystalline (or glassy) material, which appeared to be quite angular and slightly brown in colour. The presence of transparent material could be detected in the other metallic fragments particularly after they had been crushed.

Perhaps the strongest argument in favour of an extra-terrestrial origin is the detection of nickel in these particles. Due to a chemical method devised by Dr. J. P. Riley (Department of Oceanography, University of Liverpool), it has been possible to show a slight trace of nickel in the remnant in Fig. 1, and to be quite certain of its presence in the metal-bearing Scilly particles, using them all together.

The quantity of nickel is unknown, but from experience gained with particles of nickel-steel of given composition, it is fairly certain that in the Scilly particles the average nickel content is greater than 5 per cent.

Owing to the small quantity of material collected, it is impossible to be certain of a contribution from the Perseid shower. As emphasized by Öpik[4], it is likely that the large, and possibly continuous, fine dust deposit from the Zodiacal Cloud completely overwhelms any contribution from a meteor shower. Nevertheless, it is important to clarify this question, as Bowen[5] has given evidence of possible initiation of rainfall by meteor showers. If this extra-terrestrial material turns out to be primordial dust, a closer study of the metallic and stony material will be of great interest, as the particles should reflect conditions existing during their formation. Sampling the stratosphere would put much of this work on a surer footing.

We are indebted to Prof. K. F. Bowden of the Department of Oceanography, to Prof. W. S. Owen of the Department of Metallurgy, University of Liverpool, and to the Director General of the Meteorological Office, for facilities, and to Sir Edward Bullard of Cambridge, and Mr. B. C. Oddie of the Meteorological Office for much encouragement. We are especially grateful to Mr. W. G. Durbin, of the Meteorological Research Flight, for his participation in the experiment, and our thanks are due to several colleagues in the College of Technology, Liverpool.

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RESOLUTION OF CHLORPHENIRAMINE AND THE PHARMACOLOGICAL PROPERTIES OF ITS ISOMERS

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CHLORPHENIRAMINE maleate ('Piriton', Allen and Hanburys, Ltd.) [3-(*p*-chlorophenyl)-3-(2′-pyridyl)-NN-dimethyl propylamine maleate][1,2] is a potent antihistamine[3]. We wish to report its resolution, and the physical constants, and the pharmacological properties of its optical isomers.

Chlorpheniramine proved somewhat difficult to resolve since it forms readily crystallizable salts with only a few acids. Initial attempts to form crystalline salts from fifteen optically active acids were not successful; however, after standing for one year, a solution of the di-*p*-toluoyl-(−)-tartrate[4,5] in aqueous ethanol deposited a few crystals. These were used to seed a freshly prepared solution giving (−)-chlorpheniramine-di-*p*-toluoyl-(−)-tartrate, which, after recrystallization to constant rotation, had melting point 135–136° C., $[\alpha]_D^{21} + 57{\cdot}4°$ (*c*. 1·1 in ethanol). This gave (−)-chlorpheniramine [$[\alpha]_D^{21{\cdot}5} - 31{\cdot}6°$ (*c*. 1·8 in ethanol)], which was converted to the hydrogen maleate [melting point 114–115° C., $[\alpha]_D^{27} - 23{\cdot}7°$ (*c*. 1·2 in water)].

The corresponding antipodes were obtained from the di-*p*-toluoyl-(+)-tartrate [melting point 135–36°, $[\alpha]_D^{20} - 57{\cdot}8°$ (*c*. 1·7 in ethanol)], which gave (+)-chlorpheniramine [$[\alpha]_D^{24} + 31{\cdot}6°$ (*c*. 1·3 in ethanol)], which was converted to the hydrogen maleate [melting point 114° C., $[\alpha]_D^{20} + 23{\cdot}1°$ (*c*. 2·0 in water)].

The anti-histamine activity of each isomer and the racemate was assessed by an *in vitro* method. The antagonistic effect of each drug on the contractions induced by histamine of the isolated ileum of the guinea pig was determined following the method of Schild[6]. The results expressed as pA_2 values (2 min. drug-tissue contact) are shown in Table 1.

The (+) isomer exhibited approximately twice the anti-histamine activity of the racemate, while the (−) isomer showed only about half the activity of the racemate. Further studies in which the pA_2 values of the drugs were assessed after 4 and 8 min. contact with the tissue showed that the duration of the anti-histamine action of neither isomer differed from that of the racemate.

Table 1

Compound	Anti-histamine activity pA_2 value (2 min. drug–tissue contact)
(+)-Chlorpheniramine maleate	8·47
(±)-Chlorpheniramine maleate	8·10
(−)-Chlorpheniramine maleate	7·81

The acute intraperitoneal toxicity of the racemate and isomers was studied in mice. Low doses of both racemate and isomers showed no observable reactions; however, high doses produced clonic convulsions followed by depression and death. Mortality was observed for seven days after administration of the drug. These results, expressed as the *LD*50 value in mgm./kgm. for each anti-histamine, are shown in Table 2. It is apparent that the acute toxicity of each isomer does not differ significantly from that of the other, nor from that of the racemate.

Table 2

Compound	Acute intraperitoneal toxicity in mice *LD*50 mgm./kgm. ± standard error
(+)-Chlorpheniramine maleate	175·4 ± 9·7
(±)-Chlorpheniramine maleate	187·9 ± 6·7
(−)-Chlorpheniramine maleate	193·6 ± 7·5

Sedation is one of the more common side-effects of many of the anti-histamine drugs in clinical use; it was therefore thought worth while to determine whether the racemate or either isomer caused any depression of the central nervous system. This was achieved by examining the compounds for their effect in modifying the narcotic activity of intraperitoneal injections of pentobarbitone sodium in mice. Narcotic activity was estimated using the rotating drum method of Collier, Hall and Fieller[7]. These results are summarized in Table 3, and show that neither of the isomers nor the racemate potentiates the action of the barbiturate. In fact, all three compounds, when injected intraperitoneally at a dosage of 100 mgm./kgm. at the same time as the pentobarbitone sodium, significantly reduce the duration of the narcosis without affecting the onset.

It has been well established that many anti-histamines have a local anæsthetic action, a property that contributes to the beneficial effects of topical application of these agents in painful allergic or other dermatological conditions. In this study the local anæsthetic activity of the isomers and the racemate were determined in guinea pigs using the intradermal injection method of Somers and Edge[8]. Racemic chlorpheniramine maleate showed similar local anæsthetic activity to that of procaine hydro-

Table 3

Compound	No. of mice	Dose (mgm./kgm. intra-peritoneally)	Narcosis in mice				
			Pentobarb. sod. (mgm./kgm. intraperitoneally)	Onset (min. ± stand. error)	*P*	Duration (min. ± stand. error)	*P*
Saline	10	—	30	3·7 ± 0·5	—	16·1 ± 0·9	—
(+)-Chlorpheniramine maleate	10	100	30	3·7 ± 0·6	> 0·9	12·8 ± 1·0	< 0·05
(±)-Chlorpheniramine maleate	10	100	30	4·8 ± 1·0	> 0·3	11·6 ± 1·3	< 0·01
(−)-Chlorpheniramine maleate	10	100	30	3·8 ± 0·7	> 0·8	11·3 ± 1·6	< 0·02

chloride. The activity of the (−) isomer was approximately one and a half times, while the (+) isomer was only half that of the racemate.

It has been reported[9] that continued local use of anti-histamines may cause skin sensitization reactions. In view of the combination of potent anti-histaminic and local anæsthetic activity of chlorpheniramine maleate and its isomers, and their possible use in topical application, it was considered important to determine whether these compounds produced skin sensitivity. Formulated preparations of the racemate and the two isomers were therefore examined for their possible irritant action upon shaved rabbit skin. Each preparation contained 2 per cent of anti-histamine and was applied twice daily for two weeks. There was no evidence of any degree of skin sensitization during this time with any of the preparations. After treatment had stopped, the rabbits were exposed to sunlight and daylight for a further two weeks; at the end of this time there was no evidence of any photosensitivity reaction in the treated areas of skin.

The experiments performed indicate that the pharmacological activities of both the (+) and the (−) isomers of chlorpheniramine maleate are qualitatively similar to those of the racemate. The (+) isomer is more active than the racemate as an anti-histaminic drug, but is less active as a local anæsthetic; the reverse is true with the (−) isomer. In view of this quantitative difference in activity, it is interesting to note that the acute intraperitoneal toxicities of the compounds in mice are similar. It is proposed to compare the possible anti-tussive action of each of these isomers with that of the racemate.

While this communication was being written, the results of some pharmacological investigations on the optical isomers of chlorpheniramine were reported by Roth and Govier[10], but no details of the resolution or physical constants of the isomers were given. Anti-histamine and central nervous system activity and toxicity were investigated; our results are in agreement with theirs with the exception of the anti-histaminic activity of the (−) isomer, which was reported to be only 0·01 of that of the racemate.

We thank the directors of Allen and Hanburys, Ltd., for permission to publish this work, and Mrs. P. Hutchings, Mrs. G. Hayes, Miss R. Wilkins and Mr. R. Hornby for their technical assistance.

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MORPHOGENETIC RESPONSE OF *CITRUS* OVULES TO GROWTH ADJUVANTS IN CULTURE

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OUR understanding of the growth processes of ovules and their individual parts, namely, the integuments, nucellus, endosperm and embryo from inception to the adult stage, is incomplete. A study of the growth and differentiation of 'entire' ovules (pre- and post-pollination stages) using tissue-culture technique as a tool is of great use in unravelling the physiological and morphological changes that occur within them following pollination and fertilization. Apart from a few cursory reports, ovule culture is yet an unexplored field. White[1] and LaRue[2] secured a callus growth on the ovules of *Antirrhinum* sown in White's medium. The ovules of *Erythronium americanum* showed a four-fold increase in size and an irregular growth of their surface. With orchids, Withner[3] found ovule culture to be quite promising for shortening the period elapsing between pollination and maturation of the seed, and for hastening the production of seedlings. Recently, Nirmala Maheshwari[4] has reported that poppy ovules cultured at the 2-celled stage of the embryo on Nitsch's basic medium containing a mixture of vitamins, glycine, kinetin (0·4 p.p.m.) and indoleacetic acid (5 p.p.m.) grew to mature seeds capable of germination *in situ*.

From relevant literature, it would appear that no culture work has so far been done on ovules possessing adventive embryos. The present investigation was undertaken with the view of exploring the nature of response of ovules that are naturally polyembryonate to such growth supplements as coconut milk, tomato juice and malt extract.

Citrus microcarpa Bunge was chosen as the ovule source. The young fruits were surface-sterilized and the ovules dissected out. Ovules, in which nucellar embryos had been just initiated, were inoculated on White's medium which was used as control[5]. 3 and 5 per cent sucrose were also tried as carbon source and the growth adjuvants used were Seitz-filtered.

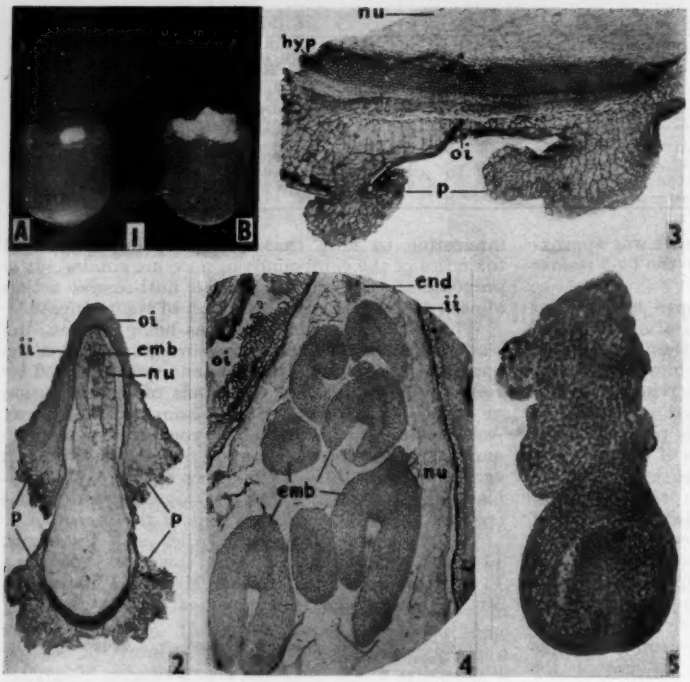

Fig. 1. *A*, two-week-old culture of ovule on White's medium + coconut milk (40 per cent). Note the hypertrophy (× *c.* 0·3); *B*, same as *A*, on White's medium + malt extract (0·5 per cent) + sucrose (3 per cent). Observe the extensive growth of fragile tissue (× *c.* 0·3)

Fig. 2. L.S. ovule from Fig. 1*B* (× *c.* 5)

Fig. 3. L.S. chalazal portion of two-week-old ovule on White's medium + sucrose (5 per cent). Note the periderm formation (× *c.* 6)

Fig. 4. L.S. micropylar part of two-week-old ovule on White's medium + sucrose (5 per cent). Note the cellular endosperm along the periphery and embryos of different stages (× *c.* 4)

Fig. 5. L.S. embryo from two-week-old ovule on White's medium + tomato juice (20 per cent), showing proliferation from basal portion (× *c.* 30)

emb, embryo; *end*, endosperm; *hyp*, hypostase; *ii*, inner integument; *nu*, nucellus; *oi*, outer integument; *p*, periderm

In all the concentrations of sucrose, the ovules swelled and showed hypertrophy of the integument accompanied by surface undulations. Later, the integument ruptured at certain places, exposing masses of glistening white tissue. The proliferations were abundant over the entire surface of the ovule except the micropylar region. In this respect 5 per cent sucrose proved superior to other concentrations.

The control medium supplemented with coconut milk (40 per cent) gave a similar response, though it was less pronounced (Fig. 1*A*). With tomato juice (20 per cent) but without indoleacetic acid and vitamins, no appreciable change in hypertrophy was noticed when compared to the control. Proliferations were, however, extensive on White's medium + 0·5 per cent malt extract (Figs. 1*B*, 2). The entire surface of the ovule showed intumescences which were of a more or less friable nature. Subcultures of such detached tissue masses did not prove successful.

Microtome sections of treated ovules revealed the following features.

The outer integument was potentially proliferative. Although no mitoses were observed, the arrangement and differentiation of the cells in a regular fashion indicated that the new tissue arose by cell divisions rather than by mere cell enlargement. The intumescent tissue originated mainly from the cambium-like cells of the sub-epidermal layers of the integument. The tissue showed 2–3 layers of tangentially elongated cells containing dense cytoplasm and a prominent nucleus. Outside these were cells which had a more vacuolate cytoplasm and degenerating nucleus; and the outermost 2–3 layers of cells were suberized. The whole structure simulated a periderm tissue (Fig. 3). In some cases isolated tracheidal cells were also found in the proliferated tissue. The inner integument did not show any response to the various treatments.

No appreciable growth of embryos was noticed in ovules cultured on White's medium containing 2 or 3 per cent sucrose. But in those on 5 per cent sucrose, the proembryos enlarged in size by cell divisions and differentiation occurred in 2 weeks (Fig. 4). However, a considerable variation in their development was met with and different stages could be seen in the same ovule. On White's medium plus tomato juice a similar response was obtained. Some embryos showed proliferations from the basal region (Fig. 5). No differentiation of embryos could be achieved either on coconut milk or malt extract.

The endosperm tissue was generally inhibited and was attenuated during development, but in ovules grown on White's medium containing varying concentrations of sucrose its growth was normal, and 2–3 layers of endosperm could be observed bordering the embryo sac. The nucellar tissue was unaffected by growth modifiers except that the cells were much elongated along the axis of the ovule.

Briefly, then, the ovules of *Citrus microcarpa* cultured on different media became hypertrophied and irregular in outline, especially so on malt extract, perhaps due to osmotic gradients in the medium. A periderm-like tissue was formed from the outer integument in almost all the treatments. It is interesting to note that proembryos when excised and cultured on White's medium showed no growth[5], whereas in cultures of whole ovules the growth and differentiation of the embryos proceeded normally. The artificial induction of budding of proembryos obtained by exogenous application of growth factors, such as tomato juice, is significant as a source of securing identical progeny.

I am grateful to Prof. P. Maheshwari and Dr. S. Narayanaswami for guidance, encouragement and helpful suggestions. Thanks are due to the Council of Scientific and Industrial Research, New Delhi, for financing a scheme of research on *in vitro* culture of plant organs under which this work was carried out.

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LETTERS TO THE EDITORS

PHYSICAL SCIENCES

Origin of the Lunar Craters and Maria

I AM prompted to tender a few pertinent comments on the recent communication by Prof. Zdeněk Kopal[1].

The physiographical similarity between many of the lunar craters and those produced by man-made explosions has been pointed out by Baldwin[2], and, if one dare assume that at least some of the lunar craters were produced by impacting objects, one can make use of this similarity and the present state of knowledge on the strong shock hydrodynamics of explosive cratering in estimating the relative energies involved and—with a slightly greater uncertainty—the masses which produced them. My own analysis, which I hope to publish shortly, leads me to believe that Baldwin's energy figures should be revised sharply upwards, that is, that the kinetic energy of an impacting mass would have to be of the order of 10^{28} ergs to produce a crater twenty miles in diameter, and one expects the diameter to vary as the cube-root of the impacting energy. While the energy partition in a venting underground explosion depends critically on the depth of penetration, present experience indicates that as much as one-half the incident energy may be absorbed in ground shock for deeply penetrating explosions. Most of this energy is absorbed in irreversible heating of the rock in a very short distance, and when the shock pressures have degraded to the order of the elastic strength of rocks (about 1 kilobar), the energy available for propagation as seismic waves is not likely to be more than 1 per cent of the incident energy.

Thus we are back again to a figure like 10^{26} ergs of seismic energy emanating from an impact capable of producing a crater 20 miles in diameter. I believe also that it is not unfair to seismologists to state that there is a disagreement of at least three orders of magnitude in the total seismic energy from the largest terrestrial earthquakes, with 10^{25} ergs as the lowest estimate. Thus it is not unreasonable to presume that the formation of a crater as large as Alphonsus would be accompanied by a moonquake of comparable intensity to the largest earthquakes, and the presence of craters twice as large as Alphonsus implies an increase of one order of magnitude in the seismic energy. In contradistinction to earthquakes, the seismic energy from an explosion is preferentially concentrated in the *P*-phase, with very little going into *S*-phase (Rayleigh waves), and the region undergoing substantial Earth motion is confined to within one or two crater radii. It appears extremely doubtful that even the largest craters, if attributable to impact, would exhibit widespread damage visible from the Earth.

With regard to conditions at the anti-focus, even if one disregards the difference in arrival times (of Rayleigh waves exclusively) due to anisotropy and non-sphericity of the lunar globe, and admits an energy concentration an order of magnitude below that at the source, there is little reason to expect any pronounced physical disturbance at the assumed caustic. The early processes in the production of seismic energy at the source are irreversible; certainly no crater would be formed. A more likely situation would be the local enhancement of ground motion, but probably never exceeding the elastic limit of the rock.

Prof. Kopal postulates that an impacting cometary mass possessing 10^{31} ergs of kinetic energy could produce 10^{20} gm. of molten lava. The results of the 'Ranier' underground atomic test in Nevada[3] indicate that less than 0·1 per cent of the total mass of material within the fracture zone was fused, and that cooling of the entire volume to temperatures like 100° C. took place in less than 1 hr. Although the equivalent of one-half the thermal energy of the bomb was required to fuse this mass of material, resolidification (if it was ever melted at all) occurred almost immediately, and the fused material was brecciated and intermingled with other debris when the cavity collapsed. In the case of a surface, or near surface, explosion, one would expect that the fused material would be thrown out of the crater along with the other debris, and not collected as a molten pool in the bottom of the crater. The distribution of fused material around the Canyon Diablo crater already supports this hypothesis.

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California. Jan. 29.

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IF Dr. van Dorn is right in concluding that the energies of meteor impacts necessary to produce lunar craters of given size are actually about 100 times larger than those postulated by Baldwin, the seismic arguments put forward in my letter of January 17 would be correspondingly strengthened; for the available estimates of the largest energies of terrestrial earthquakes range between 10^{23} and 10^{27} ergs, with 10^{25} ergs as a fair average (Gutenberg, 1958).

The fact that seismic energies of terrestrial surface explosions are spent preferentially in the *P*-waves is of no direct lunar relevance; for, first, the epicentres of lunar meteor explosions should be at least a few thousand yards deep (that is, far from pure surface phenomena in the terrestrial sense); and, secondly, the much lower gravity would allow *S*-waves on the Moon to attain greater amplitudes than on the Earth. Moreover, the real point of my communication was to direct attention, not to the damage caused by seismic waves in the immediate neighbourhood of an impact, but rather to the cumulative effects which hundreds of thousands of such occurrences would be bound to entail, and which have not been paid any attention in all previous work.

The focusing (however imperfect) of lunar *S*-waves in the anti-focal region should produce increased

fragmentation and destruction, rather than any new crater. Whether or not the elastic limit of rock could be attained remains wholly conjectural.

Lunar comet impacts and terrestrial nuclear explosions differ by so many orders of magnitude in mass, energy, as well as temperature (quite apart from different gravity and absence of atmosphere around the Moon) that scarcely any valid conclusions can be drawn from their comparison. On the other hand, to postulate the occurrence of hundreds of thousands of major meteor impacts on the Moon without simultaneous consideration of the collisions with comets would be so grossly at variance with the present frequencies of both types of bodies as to make little or no astronomical sense. As the meteor impacts on the Earth or the Moon must be accepted as facts, and their effects traced, the same must be true of the comets; and if lunar maria are not the results of such encounters, what else have comets done to the Moon?

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Low-Energy Corpuscular Radiation at High Latitudes

In high latitudes, at altitudes of order 100 km., a flux of electrons (50–90 keV.) dependent on latitude has been detected[1]. Protons of energy up to at least 90 keV. appear in auroræ[2]. I propose an explanation of this observed high-latitude corpuscular radiation on the basis of an acceleration mechanism discussed by Bohm and Gross[3].

This mechanism involves travelling (electron) electrostatic waves satisfying the dispersion relation:

$$V^2 = \frac{w^2}{K^2} = \frac{4\pi ne^2}{mK^2} + \frac{3kT}{m}$$

where V = phase velocity of the wave; w = angular frequency of the wave; K = wave number of the wave; n = electron density; e,m = charge, mass of electron; k = Boltzmann's constant; and T = temperature of region. Charged particles can be trapped[4] between the potential crests of such a wave and carried with velocity V, which increases as the wave is propagated into regions of increasing electron density.

Bohm and Gross[4] showed that electrostatic waves are infinitely damped as their wave-number approaches the lower limit $2\pi(kT/\pi^2ne^2)^{1/2}$. Hence, their band of allowable frequencies is given by:

$$\frac{4\pi ne^2}{m} \leqslant w^2 \leqslant \frac{4\pi ne^2}{m}\left(1 + \frac{3\pi}{4}\right)$$

From this it is seen that the maximum possible penetration of an electrostatic wave generated in a region of electron density n is to one of electron density $\left(1 + \frac{3\pi}{4}\right)n$.

I suggest that electrostatic waves are generated in the exosphere by solar corpuscular streams. The waves are propagated along the geomagnetic field lines, trapping charged particles and accelerating them down to levels where the electron density has increased by at most a factor $\left(1 + \frac{3\pi}{4}\right)$. At these levels the energy of the waves will have been fully converted to kinetic energy of particles moving down along the geomagnetic field lines.

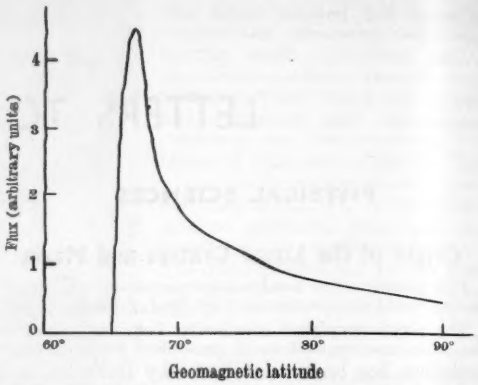

Fig. 1. Calculated variation with geomagnetic latitude of the flux of low-energy corpuscular radiation at the Earth

For purposes of calculation it is assumed that the electrostatic waves are generated at a spherical surface of radius 6·5 Earth radii and the trapping and accelerating region to be a spherical shell one Earth radius thick. Further, the flux of accelerated particles is assumed to be proportional to the volume of their trapping and accelerating region.

The calculated variation of accelerated particle flux with geomagnetic latitude is then of the form illustrated in Fig. 1. This closely fits the observations of Van Allen[1] for electron flux and resembles the latitude distribution of auroræ[5].

An estimate follows of an upper limit of the mean absolute flux, F, of accelerated protons (or electrons) at the Earth's surface. It is assumed that the energy of solar particles captured by the exosphere is fully converted to energy of electrostatic waves and then to energy of trapped particles. Hence, ignoring the kinetic energy carried by electrons:

$$sV_0\pi a^2 \times \tfrac{1}{2}mV_0^2 = F \times f \times 4\pi a^2 \times \tfrac{1}{2}mV_1^2$$

where s = number density of protons (or electrons) in the solar particle stream, V_0 = velocity of solar particles, a = radius of spherical surface at which electrostatic waves are generated, m = proton mass, f = fraction of Earth's surface on which accelerated particles are precipitated, a = radius of Earth, V_1 = velocity of accelerated particles.

Taking $s = 10$ cm.$^{-3}$, $V_0 = 10^8$ cm. sec.$^{-1}$, $V_1 = 10^9$ cm. sec.$^{-1}$, $a = 6{\cdot}5\,a$, $f = 0{\cdot}1$ (polar regions) leads to $F \approx 10^9$ cm.$^{-2}$ sec.$^{-1}$. This might be compared with the value 6×10^7 cm.$^{-2}$ sec.$^{-1}$ inferred by Chamberlain[6] for the flux of protons in auroræ and the value $10^8 - 10^9$ cm.$^{-2}$ sec.$^{-1}$ from Van Allen[1] for the flux of electrons.

From the above dispersion equation it is seen that this discussion is untenable unless $T \leqslant \frac{mV_0^2}{3k}$ in the particle-trapping region. For $V_0 = 10^8$ cm. sec.$^{-1}$ then we must have $T < 20{,}000°$ K.

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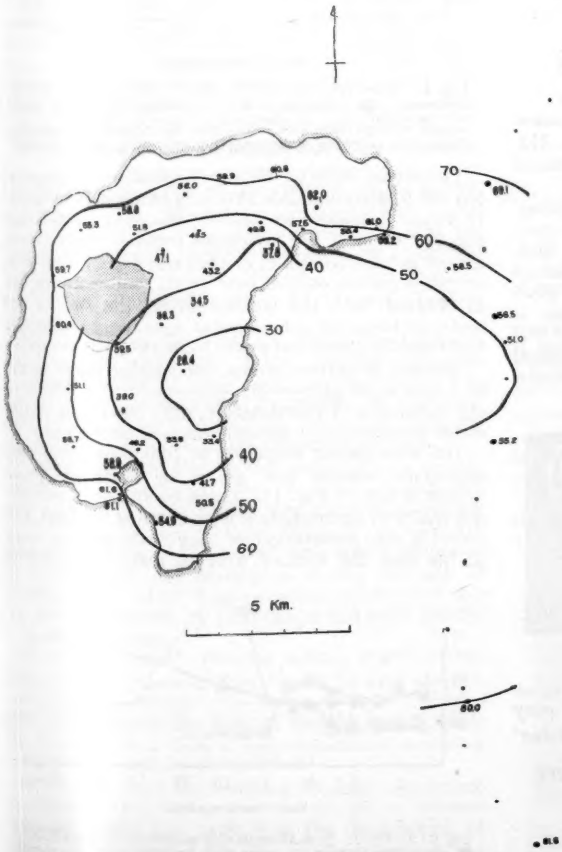
Gravity Survey on the Kuttyaro Caldera by means of a Worden Gravimeter

Lake Kuttyaro, in the eastern part of Hokkaido, Japan, is the western half of a circular caldera, which is one of the largest in the world, being about 20 km. in diameter. A small island at the centre of the lake and parasitic volcanoes in the other half of the caldera are supposed to have erupted after its formation.

At present, gravity measurement on the water is very difficult. Fortunately, we were able to use a Worden gravimeter on the surface of Lake Kuttyaro because it freezes hard in winter. It is noteworthy that the free air reduction and the Bouguer correction are uniform over the lake, and the topographical correction is very small in this region. A survey on the ice was carried out in March 1958. The Bouguer anomalies obtained on and near the lake (Fig. 1) display a relatively low anomaly of about 46 milligals, concentrated at the centre of the caldera. Comparing the distribution of the Bouguer anomalies with that of the depth of the lake (Fig. 2), it is clear that the



ig. 1. Distribution of the Bouguer anomaly (in milligals)

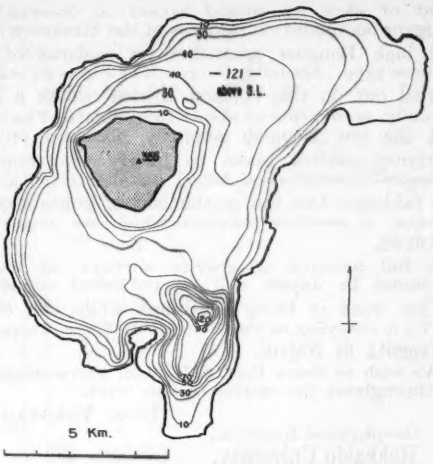


Fig. 2. Depth contours in Lake Kuttyaro (in metres)

Bouguer anomalies are almost independent of the minor structures of the surface of the ground and the depth of the lake, and must be related to the subterranean structure on a larger scale. Analysis of the distribution of the Bouguer anomalies shows that coarse material with a density about 0·3–0·5 gm./cm.^{3} smaller than that of its surroundings has accumulated at a depth of 3–4 km. beneath the lake. This coarse material is supposed to be pumice ejected during the formation of the caldera, such as is actually found widely spread over the surface of the ground in the neighbourhood. The distribution of the Bouguer anomalies gives the total mass-defect which is responsible for the low anomaly as 10^{11} tons. This value coincides with an estimate by Y. Katsui (Geological Institute, Hokkaido University), who has studied the distribution of the ejected pumice. The mechanisms by which enormous amounts of pumice were ejected and the caldera was formed cannot be elucidated by gravity survey alone, but the eruption, accompanied by the accumulation of pumice, must clearly have been so violent that the region from the surface to a depth of 3–4 km. was completely devastated.

From a petrological discussion of the pre- and post-caldera lavas, H. Kuno[1] classifies the Japanese calderas as belonging to the Krakatoa or the Glencoe types of H. Williams[2], according to the cause of their formation. An example of the former type is the Kuttyaro caldera, which collapsed into the magma reservoir accompanying the eruption of a tremendous amount of pumice; and one of the latter type is the Mihara caldera, Oosima Volcano, which was formed by the subsidence of a great mass of rocks into the magma reservoir, without the eruption of pumice. We fear that the term 'magma reservoir' in this account lacks confirmation. From this geological

point of view we should expect to observe low Bouguer anomalies on calderas of the Krakatoa type and high Bouguer anomalies on calderas of the Glencoe type. Actually, the result of a gravity survey carried out on the Volcano Mihara[3] shows a high anomaly, amounting to about 15 milligals. This fact, and the low Bouguer anomaly observed on the Kuttyaro caldera, seem to justify the proposed geological classification based on the formation of the calderas, but the mechanism of subsidence or collapse is another problem which we regard as unsolved.

A full account of gravity surveys on several volcanoes in Japan will be published elsewhere.

This work is being continued while one of us (I. Y.) is studying at the Istituto di Fisica Terrestre, Università di Napoli.

We wish to thank Prof. C. Tsuboi, who encouraged us throughout the course of this work.

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[1] Kuno, H., *Trans. Amer. Geophys. Union*, 34, 267 (1953).
[2] Williams, H., "Calderas and their Origin", Univ. Calif. Pub. Bull. Dept. Geol. Sci., 25, 239 (1941).
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Measurement of the Flocculation of Suspensions

I have read with interest the communication by R. L. Whitmore in *Nature* of January 31, p. 313, on the development of a test which was introduced by Prof. Fahraeus in 1958.

We have been using this method for testing 'Oildag' (colloidal graphite in oil, Acheson Industries (Europe), Ltd.) dispersions since 1939, and have, in fact, developed a special apparatus which allows a roll of Whatman No. 4 filter paper to be folded into a pack of 25 or more papers. The 'Oildag' concentrate is diluted with *SBP*.3 fluid, poured into the reservoir and allowed to flow through under gravity. A typical 'chromatogram' obtained by this method is shown in Fig. 1.

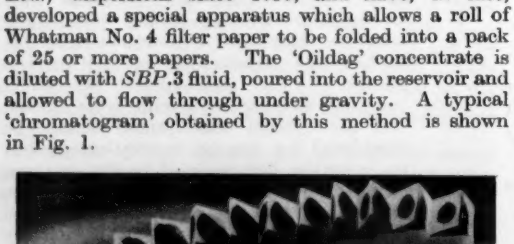

Fig. 1

I might add that we have supplied this test rig to people in many countries, as we found it a very easy method of distinguishing quickly between 'Oildag' and less stable dispersions of graphite in oil.

E. R. Braithwaite

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β-Type Interlamellar Sorption Complexes

In what we have called[1] the 'β-type' interlamellar sorption complexes of graphitic acid, the sorbed molecules are probably standing normally to the layers of the sorbate. The β-complexes with normal straight-chain amines, which we have been investigating, are particularly interesting, since they are formed over a complete range of chain-lengths.

Our new results are plotted in Fig. 1. Between 4 and 16 carbon atoms, the spacing rises linearly with the chain-length, and the slope of the line is 2·6 A. per carbon atom. This corresponds almost exactly to the projected length of two C—C single bonds, and indicates that there are two layers of sorbed molecules oriented normally to the sorbate layers. Fig. 1 shows a slight shift at 10 carbon atoms. We will not enlarge here on possible reasons for this.

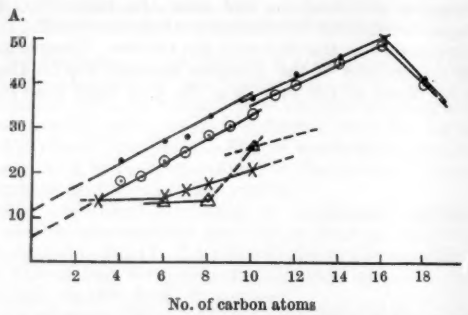

Fig. 1. Basal spacings plotted against chain-length of sorbed compound. ●, *n*-Amines with montmorillonite; ○, the same with graphitic acid; △, diamines with montmorillonite; ×, diamines with graphitic acid. Note that the diamines give half the slope of the *n*-amines, corresponding to only one layer of molecules

The actual value of the layer separation is, however, too low to accommodate two fully extended molecules. It seems necessary to assume, therefore, either that the free ends of the molecules overlap (to the same extent in each complex) or that the first two or three terminal carbon atoms, next to the amine group, are in contact with the sorbate layer, the rest of the molecule being turned around at right-angles. The last-mentioned supposition seems to us the more probable.

Beyond 16 carbon atoms, the spacing drops again, and this must apparently correspond to a tilting of the molecules. Unfortunately, only one amine in this range (octadecane-1-amine) was available to us.

We were rather surprised to find that completely analogous results are given by montmorillonite (upper graph of Fig. 1). These results are, however, not really in contradiction with those of Jordan[2], who found a flat orientation of long-chain amines, since in his case the amines were in ionic form, and in

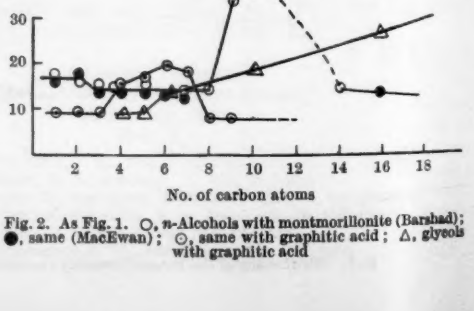

Fig. 2. As Fig. 1. ○, *n*-Alcohols with montmorillonite (Barshad); ●, same (MacEwan); ⊙, same with graphitic acid; △, glycols with graphitic acid

amounts roughly equivalent to the cation exchange capacity of the clay. In our experiments the amine was always in the form of the pure liquid. Recent work of Hofmann and collaborators[3], however, shows that even with ionic amines, β-type complexes can be formed.

Straight-chain alcohols also give β-complexes with graphitic acid, but over a much narrower range of chain-lengths (Fig. 2). These have been previously described[1], but in the light of our new results their nature becomes clearer. Barshad[4] has described what now seem to be β-type complexes formed by nonanol-1 and decanol-1 with montmorillonite. They are quite analogous to the graphitic acid complexes. Barshad's results are plotted in Fig. 2, together with ours.

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D. M. C. MacEwan

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Dundee. Jan. 29.

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Size Distribution of Tobacco Smoke Particles

Tobacco smoke from ordinary untipped proprietary branded cigarettes was collected directly on to various support films used in electron microscopy. 'Formvar' films were found to be most satisfactory in terms of particle resolution and film strength; with carbon, for example, the particles appeared to flow into one another more readily.

Smoke was allowed to impinge directly for about 5 sec. on to a 'Formvar'-covered electron microscope grid held within 1 cm. of the glowing end of a free-burning cigarette. Electron micrographs were taken at an instrumental magnification of 2,000 and the images of the smoke particles measured by an optical microscope (× 70) with a calibrated eyepiece graticule representing a spacing of 0·14μ on the original specimens.

Fig. 1*a* shows the resulting histogram of 1,200 particles obtained from three different electron microscope fields of view (such as Fig. 2*a*). The shaded area of each column represents the standard deviation obtained by using the results sequentially as 12 random samples of 100 observations each.

The histogram of Fig. 1*b* was obtained in a similar way for smoke collected 1 cm. from the mouth end of a cigarette (Fig. 2*b*). This was effected by puffing air from a small hand bellows through the cigarette from the burning to the mouth end, which simulates to some extent the conditions during the act of smoking. The extra dust particles observed in this case are recognizable by their shape and were ignored in the size analysis.

In order to test the filtering action, if any, of the lungs, the histograms of Figs. 1*c* and 1*d* were plotted, each of 800 particles. The former resulted from a brief inhalation, at the normal breathing-rate, while the latter resulted from a deep inhalation involving holding the breath for about 2 sec.

Although it may be tempting to draw immediate conclusions from histograms 1*a* to 1*d*, it became apparent during this work that the distribution of particle-size depended on the average age of the particles. As the age of the smoke increased, the particles tend to coalesce giving a greater proportion of larger particles at the expense of smaller particles, a fact easily demonstrated by collecting the smoke at different distances from the burning end of the cigarette.

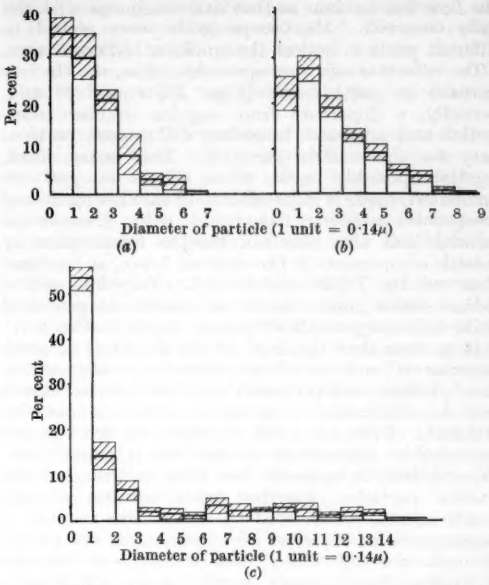

Fig. 1. Histograms showing particle-size distribution of tobacco smoke: (*a*) smoke taken directly from glowing end; (*b*) filtered through cigarette; (*c*) held briefly in lungs; (*d*) inhaled deeply

In order to obtain measurements of the aging of smoke, a glass tube, 10 ft. long and 2 in. in diameter, containing small ports at 1-ft. intervals along its length, was arranged horizontally and smoke from the glowing end of a cigarette was drawn at a speed of 1 ft./sec. along the tube by a pump at the other end.

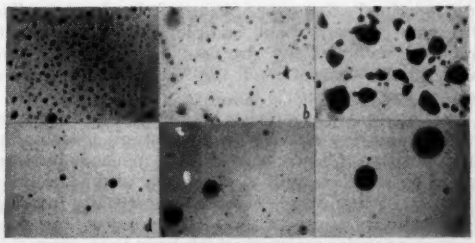

Fig. 2. Electron micrographs of tobacco smoke (× 700): (*a*) smoke taken directly from glowing end; (*b*) filtered through cigarette; (*c*) sedimented for several hours; (*d*), (*e*), (*f*) effect of aging for 1, 5, and 9 sec., respectively

The flow was laminar so that little exchange with the walls occurred. Microscope grids were placed in different ports to collect the smoke at different ages.

Two effects of age were apparent: first, the obvious increase in particle-size (Figs. 2*d*, *e* and *f*) and, secondly, a departure from regular circular cross-section and a greater boundary diffuseness, particularly for the smaller particles. This latter effect, together possibly with other effects as yet not elucidated, made it impossible to obtain histograms of acceptable consistency from field to field. Experiment showed that this was not due to evaporation of volatile components in the electron beam, as has been observed by Trillat and Cuzin[1]. Very long-period sedimentation under static air conditions produced quite different particle shapes, as shown in Fig. 2*c*.

It is clear that the 'age' of the smoke is of great importance, and its effects must be clearly understood before interpretation of distribution curves may be attempted, a situation which is not yet attained. Even so, 1,000 observations are too few for reliable conclusions to be drawn from them. Nevertheless, it appears that some filtering of the smaller particles, together with increase of size due to aging, is indicated by the greater number of larger particles observed after the smoke has passed through the cigarette; also subsequent inhaling of smoke into the lungs causes the particle sizes to be redistributed in a different way, possibly by removal of the particles of size $\sim 0{\cdot}3\mu$.

It is noteworthy that only very rarely are droplets observed surrounded by a cloud of small satellites as occurs in many of the beautiful photographs presented by Kahler and Lloyd[2]. Such satellites, we believe, are essentially a product of the electrostatic precipitation technique employed, which is therefore unsuitable for determination of particle-size.

Helpful discussions with Mr. A. Horseman of the Imperial Tobacco Co. (of Gt. Britain and Ireland), Ltd., are gratefully acknowledged.

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H. F. Kay

H. H. Wills Physics Laboratory,
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[1] Trillat, J. J., and Cuzin, J., *C.R. Acad. Sci., Paris*, **246**, 1040 (1958).
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Detecting Volatile Airborne Droplets

Liddell and Wootten[1] have described a method for sampling fog droplets in a suitable form for measurement under the microscope. In this, microscope slides were coated with a gelatin film which incorporated a purified dye. When water droplets impinged on this film a characteristic dark crater-like ring remained after evaporation of the droplet. The film gave a permanent sample and when ideally prepared detected fog droplets down to 1μ. The ratio of the diameter of the ring to the original droplet was constant.

I have recently found that by eliminating the rather troublesome dye and viewing the pure gelatin film with positive phase-contrast the method becomes one of extreme reliability, simplicity and sensitivity. (Fig. 1*a*. These droplet traces are virtually invisible with ordinary illumination.) To support the film, microscope slides are used which have been cleaned in a hot acid cleaning mixture (for example, chromic–sulphuric) and stored in 'Tergitol' solution. A slide

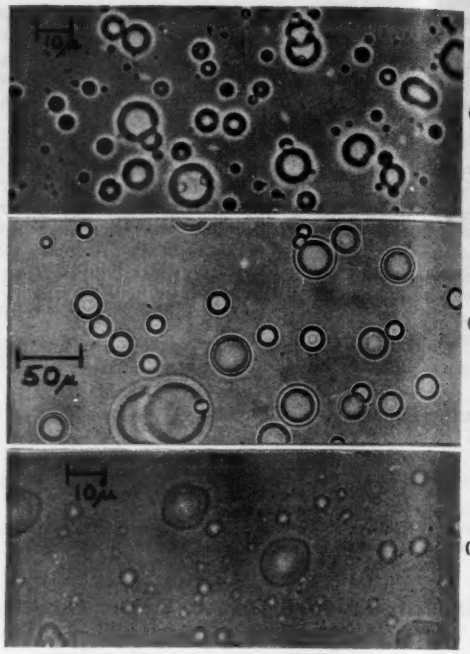

Fig. 1. Photomicrographs of traces left by volatile droplets. Scales refer to the original droplet diameters, not to the trace diameters. The samples were taken in a special form of two-stage reciprocating-slide impactor. (*a*) Fog droplets from second stage of impactor; impacting jet velocity, 60 m.p.h.; objective, 4-mm. phase-contrast. (*b*) Fog droplets from first stage of impactor; jet velocity, 5 m.p.h.; objective, 8-mm. phase-contrast. (*c*) Kerosene droplets on *R*230 silicone resin; second stage of impactor, 60 m.p.h.; objective, 8-mm. phase-contrast

is wiped dry with a clean cloth and a thin film of a warmed gelatin solution of about 5 per cent concentration is spread evenly with a glass rod. The slide is gently heated until the film is quite dry, when it is ready for use.

For the smallest droplets, say $< 10\mu$, the thickness of the dry film does not seem to be critical, but for larger droplets the thickness is optimal at about 1μ (which can be judged by the interference fringes) as thinner films give very faint rings and thicker ones may give rather confusing halo effects as in Fig. 1*b*.

As an alternative to glass, films of clear gelatin on a clear flexible base may be obtained from photographic film manufacturers and are useful when curved impingement surfaces are required. Gelatin films may be used repeatedly or rejuvenated after long storage by rinsing quickly with distilled water and re-drying.

The method is of greatest value for droplets $< 10\mu$ where other methods such as the widely used magnesium oxide method[2] or impingement into oil or grease become unreliable. Sharp images of the traces of droplets well below 1μ in diameter are seen in Fig. 1*a*. It will be noted that in counting and sizing work, overlapping traces give no trouble except when a large drop completely overlaps and obliterates a small trace. For droplets $> 10\mu$ phase-contrast illumination is not essential, but the gelatin film method is not necessarily superior to the magnesium oxide method in this range.

In work in actual fogs using a special form of droplet impactor, as will be reported elsewhere, a factor was found for drop diam./ring diam. of 0·59, in agreement

with laboratory calibration. In local fogs the method has revealed large numbers of droplets in the 1μ region as in Fig. 1*a*. A valuable feature is that the perfect optical quality of the gelatin film enables the insoluble content of the droplets, such as their condensation nuclei, to be seen and counted. The plurality of such particles in most droplets more than a few microns in diameter suggests that collision and coalescence of fog droplets is very common. A 50μ droplet may contain 50 or 100 discrete insoluble particles of 1μ or less.

Obviously, the principle of the water-sensitive gelatin film should be applicable to the detection of volatile droplets of other liquids, provided that a clear film, soluble in that liquid, can be prepared. A requirement known to me was the detection of kerosene droplets in combustion chambers. Screening tests of many kerosene-soluble substances were carried out and a satisfactory film was found in silicone resin *R*230 (I.C.I., Ltd.). This is spread on a slide and heated off in exactly the same way as for gelatin film. Contrast of the kerosene droplet traces after evaporation is not quite so good as for water on gelatin, but the phase-contrast microscope enables the traces to be seen clearly down to 2μ diam., representing droplets of 0·8μ, as the droplet/ring factor in this case is 0·4 (Fig. 1*c*).

There is no reason to doubt that suitable clear, soluble films could be found for the detection of a wide range of volatile liquids in the manner described.

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Microbiological Research Establishment,
Ministry of Supply,
Porton, Wiltshire.
Feb. 11.

[1] Liddell, H. F., and Wootten, N. W., *Quart. J. Roy. Meteor. Soc.*, **83**, 263 (1957).
[2] May, K. R., *J. Sci. Instr.*, **27**, 128 (1950).

Light Emission from Insulating Liquids due to Excitation by d.c. Fields near Breakdown

In scintillation counter applications[1,2], it is well known that dilute solutions of fluorescent organic materials, such as anthracene, in suitable organic solvents will absorb radiation and re-emit at a wave-length characteristic of the solute, when the liquid is excited by ultra-violet or high-energy particles.

While investigating pre-breakdown pulse activity and conduction currents in highly degassed and dehydrated transformer oil of Peruvian origin, it was found that visible light was emitted from the high-stress region at d.c. fields in excess of 600 kV./cm. So far as I am aware, this has not been observed previously in organic liquids. Tests were carried out in uniform fields between 1-cm. diameter nickel and stainless-steel electrodes, with a gap spacing of 89μ. The colour and frequency of the emitted light were similar to the blue fluorescence observed when the oil was excited with an ultra-violet source.

No detailed chemical results are available on the composition of the oil; but it is known that traces of unsaturated polycyclic aromatic compounds are present, and that these give rise to the fluorescence of the oil. In order to test the suggestion that light emission was due to excitation of molecules of this type, observations were made using spectroscopic grade hexane, and hexane samples doped with scintillation grade anthracene and *p*-terphenyl, dissolved at a concentration of 1 gm./l. No visible light was observed with pure hexane up to fields of 1·1 mV./cm., but light emission, characteristic of the dissolved impurity, was observed in the doped hexane samples.

Microscopic observations of this emission showed, for stresses from 600 to 950 kV./cm., filamentary luminous streamers which completely bridged the oil gap from cathode to anode, with no apparent change in intensity along its length. At higher stresses, the glow appeared to become diffuse over the high-field region.

The light intensity was found to increase in an exponential manner with increasing field, but no noticeable change occurred in the spectrum of the emitted light. Removal of the impurities was found to increase the breakdown strength. For example, fractional distillation of the oil, thus removing most of the fluorescent impurities, raised the breakdown strength of the degassed oil from 1,100 to 1,300 kV./cm. Similarly, the breakdown strength of the doped hexane was raised from 700 to 1,050 kV./cm. by removal of the added impurity.

It is possible that the light emission was due to micro-discharges in the oil rather than excitation of the fluorescent impurities in the liquid phase. By means of a metal bellows, pressure and tension was applied to the liquid in the test cell. No variation in the light intensity was observed, and fracture of the liquid did not occur when the liquid was subjected to tension at pre-breakdown fields in excess of 1,000 kV./cm.

These experiments indicate that fluorescent impurities, such as anthracene, which absorb energy by resonance of electron orbitals into higher states, may be excited by high d.c. fields in the liquid phase, and that the processes involved play some part in the processes which lead to electrical breakdown.

Acknowledgments are made to Prof. Humphrey Davies for the provision of facilities, to Dr. H. Tropper and colleagues of the Dielectrics Team for encouragement and discussion, and to the University of Queensland for the award of a Travelling Research Fellowship.

M. Darveniza

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London, E.1.
Feb. 5.

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CHEMISTRY

Analysis of Hydrocarbons

The difficulty of separating a mixture of ethane, ethylene, propane and propylene on a single column in gas-phase chromatography has been commented on recently[1]. Drs. Barnard and Hughes also mention the difficulty of using some two-stage columns. This mixture can in fact be readily separated on a single column. If it is required to analyse only small samples, a column packed with alumina may be used, either thermostatted at one temperature[2] or by 'temperature-programming' the column[3]. When both

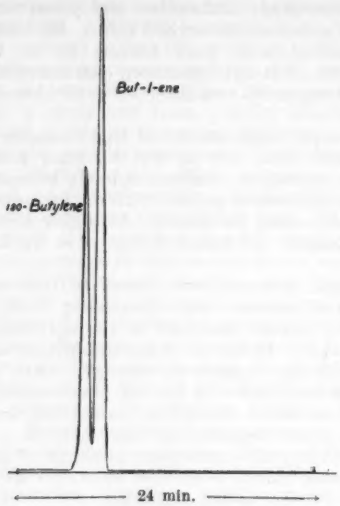

Fig. 1. 25-ft. acetonylacetone column; 0° C.; flow gas, hydrogen, 30 ml./min.

small and large samples have to be analysed, it is an advantage to use gas – liquid chromatography, and a single column of dimethylsulpholane on firebrick may be used[4]. Two-stage columns have also been used successfully to carry out this separation[4]; further, a commercial column is manufactured with which this analysis can be carried out[5].

In this laboratory this mixture has been analysed repeatedly on a single column, packed with acetonylacetone on firebrick (a copper coil, 25 ft. × ¼ in.) operated at 0° C. This column not only resolves the hydrocarbons mentioned, but also resolves nearly all the possible isomers of the C_2 to C_5 hydrocarbons, including many cyclic isomers, in a total running time of 1 hr. The column may be used to carry out the difficult analysis of *iso*butylene and but-1-ene in the presence of the other hydrocarbons. Fig. 1 shows the resolution obtained with this column and a mixture of *iso*butene and but-1-ene.

This column does not resolve 1,1-dimethyl*cyclo*propane and 3-methyl but-1-ene, two compounds which have closely similar boiling points. However, these compounds are easily separated using a solution of silver nitrate in ethylene glycol on fireclay. No difficulty has been experienced in using a short glass column (3 ft. × ¼ in.) packed with this material and attached to the end of the acetonylacetone-packed column. Such a double column allows this difficult separation to be carried out and still allows the other

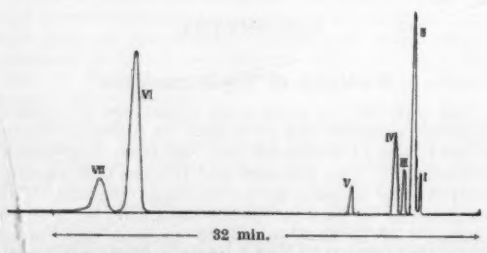

Fig. 2. Double column: 0° C.; flow gas, hydrogen, 30 ml. per min. I, Ethane; II, ethylene; III, propane; IV, propylene; V, *n*-butane; VI, 1,1-dimethyl*cyclo*propane; VII, 3-methylbut-1-ene. Ethylene peak has been attenuated by a factor of 10

C_2 to C_5 hydrocarbons to be separated (see Fig. 2). A mixed column of these two packings has been used successfully, but was found to have a relatively short 'life' when compared with the double column.

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Jan. 28.

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[4] Fredericks, E. M., and Brooks, F. R., *Anal. Chem.*, **28**, 297 (1956).
[5] Hausdorff, H. H., ref. 3, p. 377.

Dr. Frey's letter is of considerable interest. We were, of course, aware of several methods reported in the literature for the separation of the C_2 and C_3 hydrocarbons. However, the purpose of our original communication was to direct attention to a *simple* method of separating the lower hydrocarbons, not involving any of the complexities of very long coiled columns, temperature programming or the necessity of maintaining temperatures below the ambient.

Our experiences with series columns had not been particularly successful, but the experiments with the *mixed* columns, using the same preparations of packing materials and identical packing procedures, were so fruitful that we thought it worth while directing attention to what was, to us at least, a new technique.

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London.

Structure of 'Cystine Disulphoxide'

Although the reactions of aromatic 'disulphoxides' have been studied by Smiles and his co-workers[1] and by Vinkler and Klivenyi[2] among others, the structures of these compounds remained uncertain until their infra-red spectra were examined by Cymerman and Willis[3]. The latter work confirmed earlier evidence that the compounds hitherto known as disulphoxides should be assigned the thiolsulphonate structure (I) rather than the disulphoxide structure (II).

$R—SO_2—S—R$ (I) $\qquad$ $R—SO—SO—R$ (II)

Grishko and Guryanova[4] have recently made a study of some aliphatic analogues and conclude that they also have structures of type (I). The best-known aliphatic 'disulphoxide' appears to be that from cystine and this compound was assigned a structure of type (II) on chemical evidence[5], a structure which is still current in recent biochemical literature[6]. In connexion with other work we have obtained the infra-red spectrum of this compound and find it to have the characteristics of a thiolsulphonate rather than a disulphoxide. The strong bands at 1,110 cm.$^{-1}$ and 1,300 cm.$^{-1}$ agree well with those given by aromatic thiolsulphonates[3,7] and the spectrum showed no strong band near 1,050 cm.$^{-1}$ as exhibited by sulphoxides.

Using structure (II) Toennies and Lavine[5] found it necessary to introduce a series of intermediates to explain the reactions of 'cystine disulphoxide', but it is evident that these reactions can be more readily explained on the basis of structure (I). For example,

'cystine disulphoxide' reacts with cysteine to give cystine and cysteine sulphinic acid[5], and we have followed the course of this reaction by means of circular paper chromatography using *tert*-butanol – formic acid – water as solvent and ninhydrin in dry acetone as detecting agent. In our experiments the only bands appearing had R_F values of 0·00 and 0·20 (both due to cystine) and 0·35 (cysteine sulphinic acid). Examination of scale models suggests attack at the hexavalent sulphur to be sterically hindered, and in this reaction nucleophilic attack by the thiol group of cysteine might then be expected to occur at the adjacent sulphur atom, followed by fission of the SO_3—S bond of the thiolsulphonate and transfer of hydrogen. Other reactions of the thiolsulphonate can mostly be explained in a similar manner.

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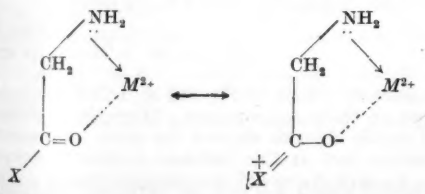
BIOCHEMISTRY

Relationship between Proton and Metal Binding by some Peptides, Amino-acid Amides and Amino-acids

The stability constants of a series of ligands of the type, $NH_2.CH_2.CO.X$, with the ions Cu(II), Co(II) and Mn(II), have been measured in this laboratory[1], and it has been shown that, for any one of the metals, a linear relationship exists between log K_1 (first stability constant) and pK_a (acid dissociation constant of the amino-group)[2]. The group X can have a variety of structures ranging from O^- (glycine) to NH_2 and $NH.CH_2.COO^-$ (glycinamide and glycylglycine). From these observations it was concluded that the structure of the metal complexes was best represented thus :



For Cu(II) this structure only applies to the complexes initially formed, prior to the onset of additional acid dissociations which occur for some of the ligands.

The structure of peptide – metal complexes is of considerable importance in understanding the mode of action of proteolytic enzymes, and it is evident that additional experimental work is urgently required in this field. The formulation given above is consistent with infra-red measurements on urea complexes[3], but the only evidence for it is indirect and based on the observed relationships between log K_1 and pK_a. Since these types of correlation can, in some circumstances, be fortuitous[4], it was considered necessary to see if similar relationships occurred in other related series of ligands.

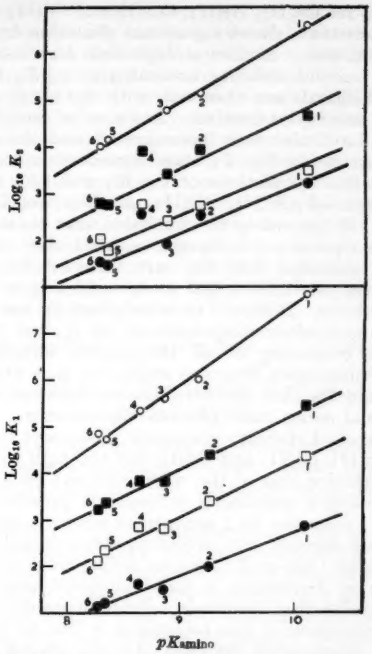


Fig. 1. Plots of log K_1 and log K_2 against pK_a for a series of sarcosyl compounds. ○, Cu(II); ■, Ni(II); □, Co(II); ●, Cd(II) (log $K_1 - 1$). 1, Sarcosine; 2, sarcosylsarcosine; 3, sarcosine dimethylamide; 4, sarcosyl L-leucine; 5, sarcosine amide; 6, sarcosine methylamide

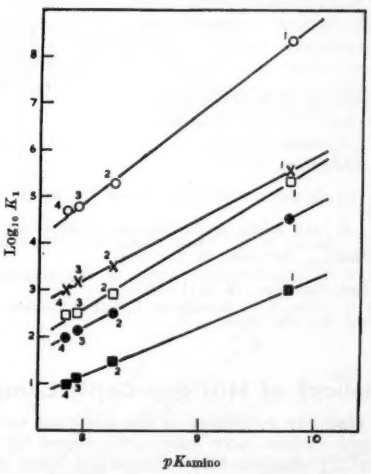


Fig. 2. Plots of log K_1 against pK_a for a series of leucyl compounds. ○, Cu(II); ×, Ni(II); □, Zn(II); ●, Co(II); ■, Cd(II) (log $K_1 - 1$). 1, Leucine; 2, leucylglycine; 3, leucylglycylglycine; 4, leucine amide

The results obtained for a series of sarcosyl ligands, $CH_3.NH.CH_2.CO.X$, are shown in Fig. 1. It can be seen that a linear relationship exists between log K_1

and pK_a for Cu(II), Ni(II), Co(II) and Cd(II); none of the constants shows significant deviation from the regression line. Similar straight-line correlations of log K_2 (second stability constant) and pK_a for the sarcosyl ligands are observed, with the single exception of sarcosyl L-leucine. A series of leucyl compounds have also been investigated and the results are illustrated in Fig. 2; these ligands show excellent straight-line correlations of log K_1 and pK_a for the complexes of Cu(II), Ni(II), Zn(II), Co(II), and Cd(II). It can safely be concluded that these linear relationships are not fortuitous, and they provide further evidence that the structures of the metal complexes of peptides and amino-acid amides are as shown above. It should be noted that, for any metal ion, a linear relationship between log K_1 and pK_a for a series consisting of all the glycyl, sarcosyl and leucyl compounds does not exist, nor is it expected. This suggests that the correlations observed for the individual series have physical significance.

The second stability constants of sarcosyl L-leucine with Ni(II), Co(II) and Cd(II) are too high to fall on the regression line of the other sarcosyl compounds. Presumably a stabilizing influence is present in the sarcosyl L-leucine 2 : 1 complexes which is absent in the other ligands and in the sarcosyl L-leucine 1 : 1 complexes. Sarcosyl L-leucine differs from the other ligands in possessing a large aliphatic side-chain; it is possible that the abnormally high stability of the 2 : 1 complexes of this compound is due to Van der Waals interactions between the side-chains of the pair of ligands co-ordinated to the metal. If so, the difference between the observed and predicted values of log K_2 gives a measure of the free-energy change associated with this interaction in aqueous solution; further investigations of this problem are intended.

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Multiplicity of Histidine–Cu(II) Complexes

The stability constants of the histidine complexes of several metals have been determined by several workers[1–4]. Satisfactory values of the stability constants can be calculated from titration data for all the metals investigated except Cu(II). Albert[3] suggested that the anomalies in the histidine – Cu(II) system are due to the planar configuration of cupric complexes in solution, which makes it impossible for all the three sites available for co-ordination (amino, imidazole and carboxyl) to be bound simultaneously to the metal ion. It has been shown[5] that other anomalies also occur in the co-ordination of Cu(II) by histidine.

If the titration curves of histidine hydrochloride in the absence and presence of equimolar cupric chloride are compared (Fig. 1), it can be seen that the

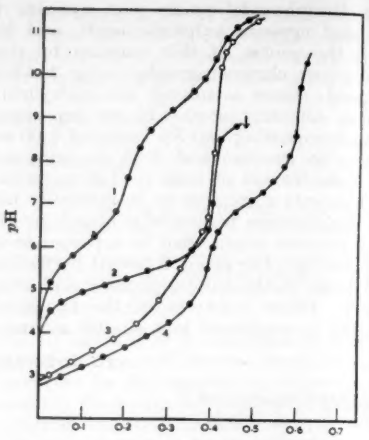


Fig. 1. Titration curves of histidine hydrochloride (0·2 mM) with sodium hydroxide (0·1 N): 1, no additions; 2, plus 0·2 mM cobalt chloride (for comparison); 3, plus 0·1 mM cupric chloride; 4, plus 0·2 mM cupric chloride

presence of Cu(II) produces one additional equivalent of acid. When the ligand – Cu(II) ratio is 2 : 1, the amount of base required to titrate all the acid species is the same as in the absence of metal. This means that an acid dissociation occurs from the 1 : 1 complex which is suppressed when the ligand to metal ratio is 2 : 1. These observations suggest that the additional acid ionization occurs from a water molecule co-ordinated to the copper atom of the 1 : 1 complex.

Attempts were made to calculate the stability constants on the assumption that the following equilibria were involved:

$$\text{For 1 : 1 mixtures, } Cu^{2+} + L^- \overset{K_1}{\rightleftharpoons} CuL^+ \quad (1)$$

$$CuL^+ \overset{K_{c'}}{\rightleftharpoons} CuL + H^+ \quad (2)$$

$$\text{For 2 : 1 mixtures, } Cu^{2+} + L^- \overset{K_1}{\rightleftharpoons} CuL^+ \quad (1)$$

$$CuL^+ + L^- \overset{K_2}{\rightleftharpoons} CuL_2 \quad (3)$$

where $K_1 = \dfrac{[CuL^+]}{[Cu^{2+}]\,[L^-]}$; $K_2 = \dfrac{[CuL_2]}{[CuL^+]\,[L^-]}$;

$$K_{c'} = \frac{[CuL]\,[H^+]}{[CuL^+]}$$

Satisfactory values of K_1 and K_2 could not be computed on these assumptions. Mixtures of histamine and cupric chloride showed the same phenomena on titration, but in this instance consistent values of K_1, K_2 and $K_{c'}$ could be obtained (log $K_1 = 9{\cdot}44$, log $K_2 = 6{\cdot}39$, $pK_{c'} = 7{\cdot}00$). Thus the difficulties in calculating the stability constants of the cupric complexes of histidine are not due to reaction (2).

If the interactions of histidine with Cu(II) only occur at any pair of the three available binding sites, singly protonated histidine ($L^{\pm}$) can also act as a chelating species; then the structure of the 1 : 1 complex will vary with pH and the following equilibria must be considered when the ligand to metal ratio is 1 : 1 :

$$Cu^{2+} + L^{+-} \overset{K_1}{\rightleftharpoons} CuL^{2+} \quad (4)$$

$$CuL^{2+} \overset{K_e}{\rightleftharpoons} CuL^{+} + H^{+} \quad (5)$$

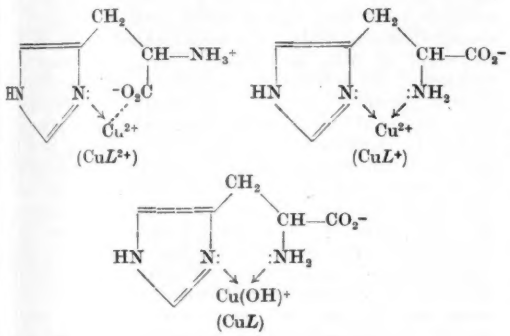
$$Cu^{2+} + L^{-} \overset{K_1}{\rightleftharpoons} CuL^{+} \quad (1)$$

$$CuL^{+} \overset{K_e'}{\rightleftharpoons} CuL + H^{+} \quad (2)$$

where $K_1' = \dfrac{[CuL^{2+}]}{[Cu^{2+}]\,[L^{+-}]}$ and $K_e = \dfrac{[CuL^{+}]\,[H^{+}]}{[CuL^{2+}]}$.

Quantitative analysis in terms of this reaction scheme yields consistent values of the equilibrium constants. The method of calculation was similar to that used for the glycylglycine – Cu(II) system[6] and will be reported in detail elsewhere. The following values were obtained: $\log K_1 = 10{\cdot}37$, $\log K_1' = 5{\cdot}02$, $pK_e = 3{\cdot}81$ and $pK_e' = 7{\cdot}19$.

The most probable structures of the 1 : 1 complexes are:



In the formation of histidine – Cu(II) 2 : 1 complexes, either of or both the ligand-chelating species (L,L^-) can be involved in interactions with CuL^{2+} and CuL^{+}. Thus there are three possible 2 : 1 complexes and the evaluation of the constants from titration data is extremely difficult.

We thank Dr. S. P. Datta for many valuable suggestions during the course of this work.

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Feedback Control of Purine Biosynthesis by Purine Ribonucleotides

In recent years a number of biosynthetic sequences have been shown to be regulated by feedback mechanisms, which have been of two general types, the first involving regulation of the activity of an enzyme by an inhibitory effect of an end-product[1,2], the second involving regulation of the rate of synthesis of an enzyme by negative-induction, or suppression, of synthesis by an end-product[3,4]. In both types of mechanisms the inhibition involves the earliest step leading specifically to the synthesis of the regulating compound, which is itself a product normally present in the cell in appreciable concentration[1,2].

The existence of feedback control mechanisms in purine biosynthesis has been suggested by a number of observations, summarized elsewhere[5,6]. In these studies the presence of unlabelled purines suppressed *de novo* purine synthesis from labelled precursors. In no instance, however, was a precise characterization or localization of the control mechanism demonstrated.

In the biosynthesis of purines the first irreversible and specific step is that in which β-phosphoribosylamine is generated from α-phosphoribosylpyrophosphate and glutamine[7–9]:

$$\alpha\text{-phosphoribosylpyrophosphate} + \text{glutamine} + \text{water} \xrightarrow{Mg^{2+}} \beta\text{-phosphoribosylamine} + \text{glutamic acid} + \text{pyrophosphate}$$

The enzyme catalysing this reaction, phosphoribosylpyrophosphate amidotransferase[9], would appear to be a likely site for the operation of a feedback control.

We have purified α-phosphoribosylpyrophosphate-amidotransferase from the supernatant fraction of pigeon liver, by fractionation with ammonium sulphate, differential heat inactivation[9], and adsorption on to, and elution from, aged calcium phosphate gel. The reaction was followed kinetically by observing the rate of generation of glutamate, measured as reduction of the 3-acetyl pyridine analogue of diphosphopyridine nucleotide, in the presence of glutamic dehydrogenase[10], in 0·05 *M* *tris*(hydroxymethyl) aminomethane buffer, *p*H 8·0.

Evidence was secured for non-consecutive binding of α-phosphoribosylpyrophosphate and glutamine at independent binding sites. When concentrations of the former and of glutamine were varied independently at four levels each, and the velocity data plotted according to Frieden[11], the lines converged to a single

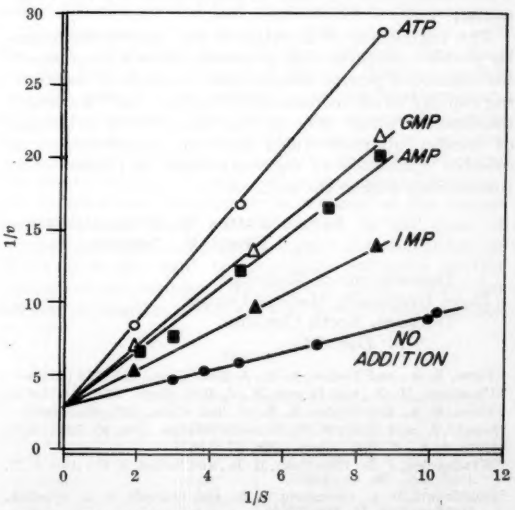

Fig. 1. Dependence of reaction velocity upon concentration of α-phosphoribosylpyrophosphate, and effect of inhibitors. Velocity was measured as increase in absorbance at 363 mμ per 10 min.; substrate in μmoles per ml. In all cases inhibitors were added in final concentration of 0·2 μmole per ml. Reactions were followed according to the standard assay, at room temperature, in 1-ml. quartz cells having a light path of 1 cm.

intercept on the extended X-axis in each case; that is, when S = α-phosphoribosylpyrophosphate, at various glutamine-levels, and when S = glutamine, at various levels of α-phosphoribosylpyrophosphate. The K_m for α-phosphoribosylpyrophosphate was $2{\cdot}3 \times 10^{-4}$ M and for glutamine was $1{\cdot}1 \times 10^{-3}$ M.

Many naturally occurring compounds were studied as potential feedback inhibitors of this enzyme. Inhibition was observed with 5-amino-4-imidazolecarboxamide ribonucleotide, inosine monophosphate, adenosine mono-, di- and tri-phosphates and guanosine mono- and di-phosphate. Selected results, plotted in Fig. 1, show competitive inhibition by inosine monophosphate, adenosine monophosphate, guanosine monophosphate and adenosine triphosphate of binding of α-phosphoribosylpyrophosphate by the enzyme. Average values for the dissociation constants of inhibitors are shown in Table 1. In other studies, the inhibitions were shown to be non-competitive with respect to binding of glutamine.

Table 1. Michaelis–Menten Constants of Substrates and Dissociation Constants of Inhibitors

Substrate	K_m
Phosphoribosylpyrophosphate	$2{\cdot}3 \times 10^{-4}$ M
Glutamine	$1{\cdot}1 \times 10^{-3}$ M
Inhibitor	**K_i**
Adenosine triphosphate	$3{\cdot}7 \times 10^{-5}$ M
Adenosine diphosphate	$3{\cdot}9 \times 10^{-5}$ M
Guanosine monophosphate	$8{\cdot}6 \times 10^{-5}$ M
Adenosine monophosphate	$9{\cdot}0 \times 10^{-4}$ M
Inosine monophosphate	$1{\cdot}8 \times 10^{-4}$ M
Guanosine diphosphate	$3{\cdot}8 \times 10^{-4}$ M

Several related compounds were shown not to inhibit this enzyme. They included deoxy-adenosine monophosphate, deoxy-guanosine monophosphate, adenosine monophosphate-2′,-3′, inosine di- and tri-phosphate, guanosine triphosphate and ribose 5-phosphate, as well as purine bases and ribonucleosides and pyrimidine ribonucleoside monophosphates and triphosphates, and inorganic pyrophosphate. Thus, the inhibitory effects described would appear to be rather specific for certain purine ribonucleotides, of which adenosine di- and tri-phosphates are the most potent.

The regulation of activity of the amidotransferase by purine ribonucleotide products offers a mechanism for control of purine biosynthesis capable of responding rapidly to environmental changes. Such a control mechanism would account for the orderly synthesis of purine ribonucleotides and the maintenance of relative constancy of concentrations of purine ribonucleotides within the cell.

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Effect of Substitution in the Side-Chain on β-Oxidation of Aryloxy-alkylcarboxylic Acids by *Nocardia opaca*

The rate of β-oxidation of γ-substituted butyric acids by washed suspensions of species of soil *Nocardia* has been found to depend on the nature of the substituents[1,2]. γ-Phenoxybutyric is oxidized more slowly than γ-phenylbutyric acid, and substitution in the phenoxy group, particularly in the *ortho* position, further retards the process. β-Hydroxy acid intermediates were generally formed from γ-aryloxybutyric acids. It has now been found that the substitution of CH_3— for H— on the γ carbon atom of the γ-phenoxybutyric acids further retards β-oxidation.

In this work washed suspensions of *Nocardia opaca* (strain T_{16}), and the techniques of paper chromatography and infra-red analysis previously described[1] were used to study the conversion of DLγ-phenoxy-γ-methylbutyric, DLα-(4-chloro-2-methylphenoxy)-α-methylacetic, DLγ-(4-chloro-2-methylphenoxy)-γ-methylbutyric and DLε-(4-chloro-2-methylphenoxy)-ε-methylcaproic acids. We are indebted to Dr. B. J. Heywood of May and Baker, Ltd., for generous supplies of the first three compounds. DLε-(4-chloro-2-methylphenoxy)-ε-methylcaproic acid was prepared from DLγ-(4-chloro-2-methylphenoxy)-γ-methylbutyric acid by reduction to the alcohol (b.p. 146° C. at 0·1 mm.) with lithium aluminium hydride and formation of the bromide (b.p. 127° at 0·4 mm.) with phosphorus tribromide followed by condensation with malonic ester (in butanol). The dibutyl ester obtained decomposed to some extent on distillation, and the crude DLε-(4-chloro-2-methylphenoxy)-ε-methylcaproic acid obtained by hydrolysis and decarboxylation in the usual way was purified by conversion to the ethyl ester (b.p. 140° at 0·3 mm.) which was distilled and saponified. The syrupy product (found C, 61·35; H, 6·86, $C_{14}H_{19}O_3Cl$ requires C, 62·02; H, 7·05 per cent) gave only a single spot on the paper chromatogram, but this was not well separated from DLγ-(4-chloro-2-methylphenoxy)-γ-methylbutyric acid.

Table 1 indicates that DLγ-phenoxy-γ-methylbutyric acid is metabolized at a slower rate than γ-phenoxybutyric acid, when these substances are exposed to suspensions of T_{16} in the Warburg flask.

Table 1

Substrate	μlitres oxygen/3 hr.
None	55·7
M/250 γ-phenoxybutyric acid	123·3
M/250 γ-phenoxy-γ-methylbutyric acid	86·9

Each vessel contained 1·0 ml. cell suspension (10·6 mgm./ml. dry wt.) + 0·5 ml. M/15 phosphate buffer pH 7·2 + 0·5 ml. substrate (as sodium salt) + water to give a final volume of 2·5 ml. The centre well had 0·2 ml. 5 per cent potassium hydroxide.

Confirmation of this was obtained in a large-scale experiment in which cells were incubated with these compounds. Paper chromatography of ether extracts of suitable aliquots showed that whereas γ-phenoxybutyric acid had been completely converted in 3 days, only about 60 per cent of DLγ-phenoxy-γ-methylbutyric acid had been converted. Infra-red analysis of the final products confirmed that γ-phenoxybutyric acid had been completely converted to phenoxyacetic acid, which was isolated in crystalline form, but that 50 per cent of the product from γ-phenoxy-γ-methylbutyric acid consisted of the β-hydroxy acid. A small amount of phenoxy-α-methylacetic acid was also present. After a further addition of cells com-

plete oxidation to the acetic acid was achieved, showing that both D- and L-isomers had been metabolized.

A large-scale experiment was also set up to study the behaviour of DLα-(4-chloro-2-methylphenoxy)-α-methylacetic acid and DLγ-(4-chloro-2-methylphenoxy)-γ-methylbutyric acid. After six fresh additions of washed cells at 7-day intervals it was found that no substantial change had occurred in either. Previous work[1] with γ-(4-chloro-2-methylphenoxy) butyric acid under these conditions showed conversion to the corresponding β-hydroxy acid. The foregoing experiments clearly demonstrate that the compounds with the unbranched side-chain are much more easily oxidized than those with a branched side-chain.

This effect, as with ring substitution[1], is most marked with a short fatty acid side-chain. Thus it was found in Warburg experiments that there was a marked increase in oxygen uptake by cells of T_{16} with DLε-(4-chloro-2-methylphenoxy)-ε-methylcaproic acid when compared with DLγ-(4-chloro-2-methylphenoxy)-γ-methylbutyric acid suggesting a much more rapid breakdown of the side-chain of the former. This was confirmed in a large-scale incubation experiment where it was shown by infra-red analysis that DLε-(4-chloro-2-methylphenoxy)-ε-methylcaproic acid had been converted to DLγ-(4-chloro-2-methylphenoxy)-γ-methylbutyric acid in 4 days. In this case a crystalline product was isolated.

By analogy these results suggest that many plants which β-oxidize γ-(4-chloro-2-methylphenoxy) butyric acid will fail to convert DLγ-(4-chloro-2-methylphenoxy)-γ-methylbutyric acid to the herbicidal DLα-(4-chloro-2-methylphenoxy)-α-methylacetic acid[2].

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Crystallization of Gramicidin

Gramicidin, an antibiotic produced from a strain of *Bacillus brevis*, is reported to be soluble in the lower alcohols and to be crystallizable from dioxan and/or acetone[1-3]. With some special batches of gramicidin, Synge[4] has obtained a few crystals from ethanol after slow vapourization of the solvent.

In all manuals a melting point of 228–231° C. is quoted for crystalline gramicidin.

All batches of gramicidin so far tested by us have yielded crystals from ethanol not only after vapourization of the solvent but also on prolonged standing at room temperature.

X-ray diffraction studies of this product and of that crystallized from acetone revealed essentially the same basic picture. However, the diffraction pattern of the former was much easier to see, disclosing a larger number of lines and thus indicating better structure of crystals obtained from ethanol (Table 1).

Table 1

Line No.	Acetone form		Ethanol form	
	Distance (cm.)	Description	Distance (cm.)	Description
1-2	1·3-1·5	diffuse band	1·3	strong line
			1·5	strong line
3	1·9	very faint diffuse line	1·9	diffuse line
4		?	2·25	faint double line
5		?	2·8	faint diffuse line
6		?		?
7	3·3	diffuse band	3·4	strong line
8		diffuse band	3·65	strong line
9	3·95	diffuse band	3·95	strong line
10		?	4·1	faint line
11	4·3	double line	4·3	strong line
12	4·5	faint (double ?) line	4·6	faint line
13	4·75	double line	4·8	double line
14		?	4·95	faint line
15		?	5·28	very faint line
16		?	5·98	faint diffuse line
17		?	6·25	very faint line
18		?	6·5	very faint line
19		?	6·93	very faint line
20	7·25	faint line	7·2	very faint line
21		?	7·7	faint line
22	8·15	faint line	8·15	very faint line
23		?	8·7	very faint line
24		?	10·6	faint double line
25		?	12·1	very faint line
26		?	13·1	faint line

Further investigations revealed distinct differences in solubilities and melting points of the two 'gramicidin forms'. To obtain additional information, we have re-crystallized the 'acetone form' from a number of solvents. Some characteristics of the most thoroughly investigated products are listed in Table 2.

The solubility of four 'gramicidin forms' in 96 per cent ethanol was investigated at different temperatures (Fig. 1). In order to avoid too much interference by transformation processes in all these investigations, a short equilibration period (1-hr. shaking) had to be used. Even under such conditions, it was difficult to obtain consistent results—especially with different batches.

Recrystallization was also carried out with mixtures of solvents. The melting point followed that obtainable with the solvent last vapourized in the process.

The conclusion seems to be that the solvent used for the crystallization, or the solvent persisting longest during the process of drying, determines the melting point and the solubility of the final product. It is our impression that in the case of crystallization from acetone a considerable number of solvent molecules are embedded into the crystalline structure but removed upon drying. This is indicated both by the voluminous consistency in acetone of the slurry and the moist cake—not observed in the case of crystallization from alcohols, higher ketones, ether or cyclic solvents—and the marked influence of the drying conditions upon the melting point. Also the inferior crystalline structure and lower melting point

Table 2

Recrystallized from	Solubility at room temperature		Melting point, corrected (° C.)
	In ethanol	In methanol	
Acetone	21·0%	>25·0%	228–231* 232–235*
Methanol	3·5%	3·9%	244–247
Ethanol	3·3%	>25·0	247–249†
n-Butanol	2·4%	39·0%	246–248

* Depends on the drying conditions, the higher melting-point range being obtained in a very slow drying process.

† Recently we have obtained a melting point of 251–253° C. (corr.) with a batch recrystallized several times from ethanol.

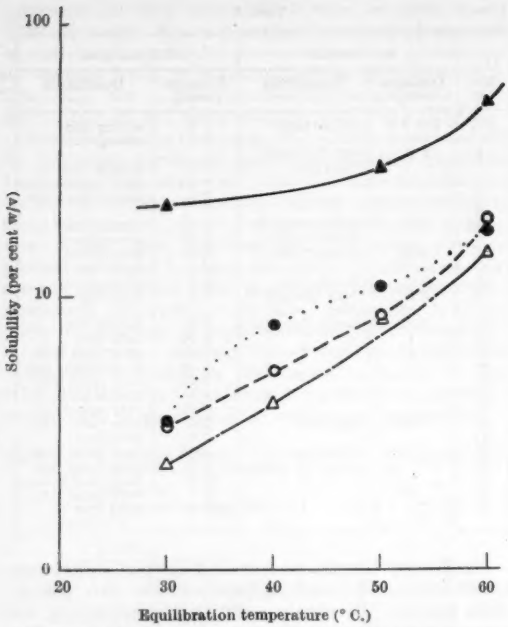

Fig. 1. ▲, Acetone form; ●, methanol form; ○, ethanol form; △, *n*-butanol form

indicate a kind of deterioration of the structure which might be due to the removal of acetone. This seems to confirm Hodgkin's[5] hypothesis, at least in the case of acetone.

The different 'forms' of gramicidin may, under proper conditions, be quantitatively (on weight as well as biopotency basis) transformed into each other.

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ANIMAL PHYSIOLOGY

Ganglionic Block and Monoamine Oxidase Inhibitors

Recently, certain monoamine oxidase inhibitors have been reported to be useful in the treatment of hypertension, and some of the clinical data suggest that ganglionic blockade may be caused by such agents[1,2]. To date, however, there have been no pharmacological studies to support these clinical impressions. In re-examining data, presented by Gertner, Paasonen and Giarman[3], demonstrating the presence of 5-hydroxytryptamine when the superior cervical ganglion was perfused with iproniazid, it was seen in these experiments that iproniazid blocked ganglionic transmission. Furthermore, a definite dosage–response relationship was found; minimal blocking effects were seen with 100 μgm. of iproniazid per ml. of perfusion fluid and complete blockade when 400 μgm./ml. was used. The appearance of 5-hydroxytryptamine in the perfusate occurred a considerable time after the appearance of ganglionic blockade. In ascertaining the effects of the *p*-tolyl ether of choline, the authors found that it, too, would block transmission, but no 5-hydroxytryptamine appeared in the perfusate.

Recently, in examining two additional potent monoamine oxidase inhibitors, β-phenyl *iso*propylhydrazine (*JB*–516, Lakeside Laboratories)[4] and the alkaloid harmine[5], it was found that both these agents blocked transmission, in a manner similar to iproniazid. When the ganglion was perfused with a Locke's solution containing 10 μgm./ml. of β-phenyl *iso*propylhydrazine, a gradual block of transmission resulted, which increased in magnitude over a period of 1 hr. This block could be reversed by reverting to drug-free Locke's solution. β-Phenyl *iso*propylhydrazine at 20 μgm./ml. produced a more rapid and greater block of transmission, and increasing the concentration to 50 μgm./ml. resulted in complete and immediate blockade, which was generally only partially reversible if the ganglion was perfused with this substance for periods of an hour. Harmine in concentrations of 10 μgm./ml. produced a block of transmission which was similar to that seen with β-phenyl *iso*propylhydrazine. This effect was gradual over a period of 1 hr. and completely reversible. By increasing the concentration of harmine to 20 μgm./ml. a complete block was observed in 15 min., which was entirely reversible. In all these experiments the *p*H of the perfusion fluid was very carefully adjusted to 7·3.

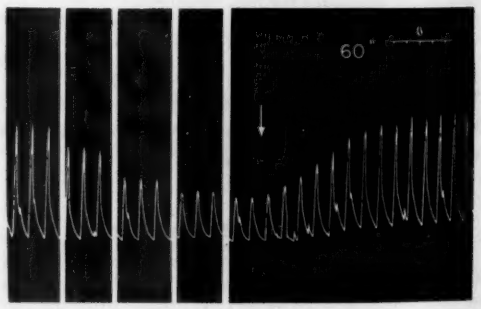

Fig. 1. Effect of harmine on the superior cervical ganglion of the cat. Contractions of the nictitating membrane to stimulation of the cervical sympathetic trunk at 0·5 m.sec., 10 c.p.s. and maximal voltage (*A*); control (*B*); 15 min. after start of perfusion with harmine, 10 μgm./ml. (*C*); 30 min. later (*D*); 1 hr. later (*E*). At arrow Locke's solution lacking the inhibitor was reinstituted

β-Phenyl *iso*propylhydrazine is a substance similar in structure to iproniazid. The action of this compound in blocking transmission would therefore appear to be analogous to the action of iproniazid, another hydrazine. Isoniazid, however, another hydrazine derivative, which lacks the ability to inhibit monoamine oxidase[6], was found to be without action on the ganglion in concentrations up to 400 μgm./ml. Harmine is of a completely different

chemical structure with no apparent relationship at all to either iproniazid or β-phenyl *iso*propylhydrazine except for its ability to inhibit monoamine oxidase.

The findings with three chemically different inhibitors—the hydrazines, the choline ether and harmine—would tend to give some support to the hypothesis that the inhibition of monoamine oxidase results in ganglionic blockade, if it could be shown that the block of transmission is always correlated with the inhibition of monoamine oxidase in the ganglion. The implication, if this be true, is that a substance is accumulating at the ganglion which can inhibit transmission and which would appear to have a function in transmission. Some evidence for such a hypothesis is that with low concentrations of the inhibitors, the block of transmission develops gradually and increases in magnitude with time. This can be contrasted with hexamethonium blockade which is immediate.

Experiments are proceeding to elucidate the mechanism of the block produced by monoamine oxidase inhibitors.

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Preparation of Cæruloplasmin from the *G2* Fraction of Human Plasma

THE recent publication of a communication on the preparation of cæruloplasmin[1], the main cuproprotein of plasma, prompts this brief account of a method of its preparation from the precipitate *G2*, the mixture of α- and β-globulins obtained in the plasma fractionation scheme of Kekwick and Mackay[2]. With *G2* from batches of plasma of 40–150 l., the following stages were used: (1) Extraction of *G2* by 0·07 *M* sodium chloride at *p*H 7 and denaturation of extracted lipoprotein with ether below − 25° C. by the McFarlane technique[3]; (2) precipitation of cæruloplasmin from the ether-saturated extract at *p*H 4·8; (3) solution of the precipitate in ether-saturated 0·1 *M* sodium chloride, removal of impurities by precipitation at *p*H 5·35 and a second McFarlane treatment; (4) reprecipitation of cæruloplasmin at *p*H 4·8 as in (2) and solution in 0·1 *M* sodium chloride; (5) precipitation of impurities at *p*H 4·8 by diluting to 0·02 *M* sodium chloride and precipitation of cæruloplasmin by further dilution to 0·0045 *M* sodium chloride. The product was dissolved in 0·1 *M* sodium chloride. $E_{1\,cm.}$ (605 mμ)/$E_{1\,cm.}$ (280 mμ), which gives a measure of degree of purification, was 0·019.

About 45 per cent of the oxidase activity of the initial extract was recovered. Stages 2 and 4 resulted in concentration rather than purification. They were necessary to reduce working volumes in the large-scale work described here, but presumably could be omitted in smaller-scale work. Further purification to $E_{1\,cm.}$(605 mμ)/$E_{1\,cm.}$(280 mμ) = 0·033 was possible using a batch adsorption method with diethylaminoethylcellulose ('DEAE' Kodak). Cæruloplasmin was adsorbed on the diethylaminoethylcellulose from 0·05 *M*, *p*H 5·7, sodium acetate buffer with 0·08 *M* sodium chloride and eluted by 0·05 *M*, *p*H 5·2, sodium acetate buffer with 0·25 *M* sodium chloride. Greater purification of the product of stage 5 was attained on a diethylaminoethylcellulose column with an elution gradient from 0·05 *M*, *p*H 5·7, sodium acetate buffer with 0·10 *M* sodium chloride to 0·05 *M*, *p*H 5·2, sodium acetate buffer with 0·25 *M* sodium chloride, using a constant-volume mixing chamber. Bulked eluate fractions were chromatographed again on a similar column. The product had a copper/nitrogen ratio of 0·0197 w/w and $E_{1\,cm.}$(605 mμ)/$E_{1\,cm.}$(280 mμ) of 0·044. This compares well with the ratio of 0·042 of purified cæruloplasmin prepared by Morell and Scheinberg[4]. The purification was performed at 2–4° C., excepting the column chromatography, which was done at room temperature. Freeze-drying of cæruloplasmin preparations resulted in partial loss of oxidase activity and markedly altered absorption spectra in the visible range unless exceptionally rapid freezing on 0·1 *M* sodium chloride was used. Freeze-drying from a salt-free solution under the same conditions caused partial inactivation. It is of interest that the cuproprotein hæmocyanin (*Busycon canaliculatum* and *Limulus polyphemus*) is also fragile under freeze-drying conditions[5].

The advantages of the method are that the raw material *G2* is plentiful, being usually discarded in the preparation of gamma globulin for clinical use; and that relatively mild *p*H and solvent conditions are used throughout. The method is suitable for large-scale work. This investigation will be described more fully elsewhere.

We thank Dr. D. R. Kominz for making available to us unpublished results on the purification of cæruloplasmin. One of us (G. C.) thanks the Research Advisory Committee of the Institute of Neurology for financial support.

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Effects of Pyridoxine Withdrawal on Cerebral Circulation and Metabolism in a Pyridoxine-dependent Child

RECENT studies have established a relationship between vitamin B_6 metabolism and convulsive disorders of the nervous system. Pyridoxine deficiency in young animals and human infants and the administration of pyridoxine antagonists in animals have been observed to cause convulsive activity which is rapidly alleviated by administration of pyridoxine[1,2]. Several instances have been reported of children with abnormally high vitamin B_6 requirements[1,3]. On ordinary dietary vitamin B_6 intake, they appear, at least as regards their nervous system,

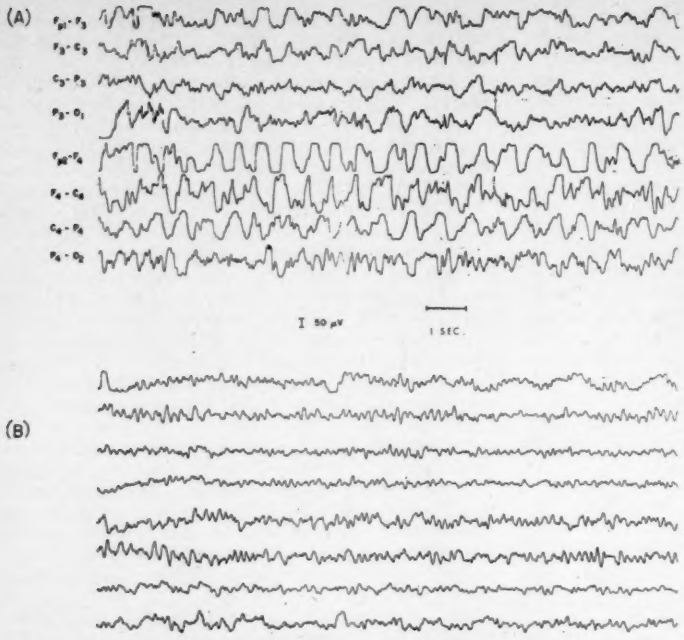

Fig. 1. Electroencephalographic tracings of pyridoxine-dependent child: *A*, 72 hr. after withdrawal of pyridoxine maintenance dose; *B*, 2 min. after intravenous administration of 15 mgm. pyridoxine to terminate seizure observed in *A*

to be suffering from a relative vitamin B_6 deficiency and are subject to convulsions which are rapidly terminated by pyridoxine administration, or entirely prevented by pyridoxine supplementation of the diet. In order to investigate further the nature of the cerebral metabolic disturbances occurring *in vivo* in vitamin B_6 deficiency, measurements of cerebral blood flow, oxygen consumption, and respiratory quotient were made in one of these pyridoxine-dependent children during a period of seizure activity induced by withdrawal of pyridoxine from the diet and immediately after its alleviation by parenteral administration of pyridoxine.

The child, a 6-year-old girl previously reported by Hunt[3], first developed seizures 4 hr. after birth. These did not respond to the usual anticonvulsant therapy but could be controlled by relatively high doses of pyridoxine. Since 2 years of age, she had been maintained free of seizures by a daily oral dose of 10 mgm. of pyridoxine. At the time of the present studies, she exhibited no gross abnormalities other than pronounced mental retardation. In preparation for the cerebral metabolic studies, pyridoxine therapy was completely interrupted, and within 72 hr. clinical and electroencephalographic evidence of seizure activity appeared (Fig. 1*A*). 15 mgm. of pyridoxine were then administered intravenously; within 2 min. all clinical manifestations of seizure disappeared, and the electroencephalograph reverted to the normal pattern (Fig. 1*B*). The same sequence was then repeated with the addition of cerebral blood flow, oxygen consumption, and respiratory quotient measurements; these were made 64 hr. after the withdrawal of pyridoxine therapy when signs of seizure activity first appeared, and then again 18 min. after the intravenous injection of 15 mgm. of pyridoxine when nervous function had been restored to normal.

Cerebral blood flow was measured by the krypton-85 modification[4] of the nitrous oxide method[5]. However, because of the child's lack of co-operation, the periods of measurement were limited to 7 min. instead of the 10 or more minutes generally recommended. This alteration can lead to approximately 10 per cent higher estimates of cerebral blood flow because of its tendency to weight slightly more heavily the contribution of the more rapidly perfused cerebral tissues, for example, grey matter; the same situation, however, would obtain in both measurements of this study. Cerebral oxygen consumption and respiratory quotient were calculated from the measured values of flow of cerebral blood and arterial-cerebral venous oxygen and carbon dioxide differences as previously described[5].

The results are given in Table 1. During the seizure, flow of cerebral blood, consumption of oxygen, arteriovenous oxygen differences, and respiratory quotient were all markedly depressed below the levels reported in normal children of this age[6]. Termination of the seizure by pyridoxine resulted in a slight rise in flow of cerebral blood, a moderate increase in consumption of cerebral oxygen, and a restoration of the arteriovenous oxygen difference and respiratory quotient to normal. Because the extreme rarity of the syndrome almost precludes further expansion of this series, any attempt to evaluate the significance of the changes must be based on the observations in this single case. The changes in flow of cerebral blood, arteriovenous oxygen difference, and respiratory quotient, were all approximately equal to the standard deviations of the differences between consecutive control measurements of these functions in normal subjects; it is therefore difficult to draw conclusions from them with any reasonable degree of confidence. The increase in consumption of cerebral oxygen, however, was equal to two such standard deviations and may be presumed to be an effect of the pyridoxine (P approx. 0·05).

During most types of convulsions, for example, those induced by electroshock[7] or analeptic drugs[8], consumption of cerebral oxygen is markedly increased and then falls to low levels in the immediate post-convulsive state[8,9]. Opposite changes, however, appear to occur in conditions like insulin hypogly-

Table 1. Cerebral Blood Flow and Metabolism during Convulsive Seizure and After Termination by Pyridoxine in Pyridoxine-dependent Child

	During seizure	After 15 mgm. pyridoxine
Cerebral blood flow (ml. blood/100 gm./min.)	63	70
Cerebral metabolic rate (ml. oxygen/100 gm./min.)	3·3	4·4
Arterial-cerebral venous oxygen difference (vol. per cent)	5·26	6·23
Cerebral respiratory quotient	0·85	0·96

cæmia[9] in which there is a deficiency of an essential substrate for the brain. The results of this study resemble those of insulin hypoglycæmia, and suggest that perhaps with pyridoxine deficiency also there is interference with the supply or utilization of an essential substrate for the brain.

The convulsions caused by pyridoxine antagonists in experimental animals have been found to be associated with a decreased level of γ-amino-butyric acid in the brain and to be arrested by administration of this compound[2]. γ-Amino-butyric acid is formed only in the central nervous system by the decarboxylation of glutamate, which is dependent on pyridoxal phosphate, but there is some uncertainty whether it functions in the brain as a neurohumoral mediator of cerebral inhibitory functions or as a substrate for metabolic oxidations[1,10]. In the former case, its deficiency might be expected to lead to convulsions with increased consumption of cerebral oxygen because of increased neuronal functional activity; in the latter, reduction in cerebral metabolic rate would be expected. The results of this study tend to support the latter hypothesis.

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Arginine Esterase Activity of 'Blood Thromboplastin'

The presence of a thromboplastin-generating system in blood has been shown by Biggs, Douglas and Macfarlane[1]. It is now recognized that at least six different factors participate in the formation of 'blood thromboplastin' and that a series of reactions resulting in the production of hypothetical intermediates such as product I and product II (Table 1) precede the appearance of the active prothrombin-converting substance[2,3].

Table 1

System	Tosyl–arginine methyl ester esterase activity
Product I Aged plasma treated with barium sulphate Serum Calcium chloride Buffer	52
Product II Product I Azolectin	71
'Blood thromboplastin' Product II Purified human plasma *Ac–G*	107

Plasma and serum components were prepared from fresh normal human blood. '*Ac–G*-free' plasma was prepared by incubating plasma for 24 hr. at 37° C. This plasma was treated with barium sulphate until it had a prothrombin time of at least 60 min. The serum was incubated at 37° C. until it did not produce a fibrin strand for 60 min. when added to purified bovine fibrinogen. A 30-mgm. per cent aqueous emulsion of azolectin (soybean phosphatides) served as a platelet substitute. Purified human plasma *Ac–G* was prepared according to Lewis and Ware (ref. 4). Suitable dilutions of the various components were made with 0·025 *M tris* buffer, *p*H 8·2. Pre-incubation of the generating systems was allowed to proceed for 6 min. at 37° C. Tosyl–arginine methyl ester esterase activity levels were determined for a 90-min. period at 37° C. using a modification of the method of Rhodes, Hill and Feeney (ref. 5).

We have found that complete thromboplastin-generating systems prepared with normal human plasma and serum components exhibit tosyl–arginine methyl ester esterase characteristics and that similar, although less marked, activities were also shown by product I and product II mixtures (Table 1). Although special precautions were taken in this work to ensure the absence of prothrombin and thrombin in both plasma and serum components of the thromboplastin-generating mixture, the possibility that a small amount of thrombin was formed during the pre-incubation of the complete system cannot be excluded.

The addition of soybean trypsin inhibitor to the complete thromboplastin-generating system following its pre-incubation resulted in marked inhibition of its tosyl–arginine methyl ester esterase activity. Essentially identical results were also obtained when the thromboplastin-generating system was made up with plasma and serum components from patients maintained on long-term prothrombin-depressant anticoagulant therapy. When, on the other hand, plasma and serum components from patients with histories of thrombo-embolic episodes were used the esterase activity still measurable in the presence of soybean trypsin inhibitor is more than twice that found with the other two groups (Table 2).

Soybean trypsin inhibitor does not interfere with the clotting activity of purified thrombin and we have

Table 2

Type of patient	Tosyl–arginine methyl ester esterase activity of 'blood thromboplastin'	Tosyl–arginine methyl ester esterase activity of 'blood thromboplastin' in presence of SBTI*
'Normal'	89 (70–127)	14 (0–36)
Long-term anticoagulant therapy	74 (53–90)	8 (0–12)
Past history of thrombo-embolism	111 (52–173)	43 (22–69)

* Soybean trypsin inhibitor

The figures represent the averages of the results obtained with six different patients in each of the three groups, and the figures in the brackets show the range of the individual determinations. Soybean trypsin inhibitor was added to the system following the 6-min. pre-incubation period to give a final concentration of 60/μgm./ml. Other details of the procedure were the same as those described in the legend for Table 1.

observed a similar lack of inhibition of the activity of its tosyl-arginine methyl ester esterase. Whether or not the thromboplastin esterase activity still measured in the presence of the inhibitor is actually due to thrombin is not known at present, although the clotting of purified fibrinogen by the complete thromboplastin-generating system suggests that this may, in fact, be the case. Evidence for the formation of trace amounts of thrombin in a similar pre-incubation system has been presented by Johnston and Jensen[6].

The findings reported here are of particular interest in view of some recent observations on differences in activities of tosyl-arginine methyl esterase of freshly collected, citrated plasmas of the same three groups of patients[7]. The possible relationship between the two sets of observations is now being studied and will be reported in greater detail elsewhere.

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Aortic Medial Calcification and Lowered Metabolism in Ground Squirrels

This study was intended to test in mammals the concept that some animals have a potential physiological limit of energy which may be utilized at different rates depending upon environmental temperatures. McArthur and Baillie[1] were able to triple the life-span of *Daphnia* (Crustacea) by a 20-deg. drop in temperature. The total heart beats during the life of the *Daphnia* differed by less than 2 per cent whether the duration of life was a few days due to high temperature or several months due to low temperature. Similarly, Carlson and Hoelzel[2] prolonged the life-span of white rats by reducing their metabolism by partial starvation.

In our investigation, two groups of thirteen-lined ground squirrels: a control group (N-14) always maintained at room temperature, and a group which hibernated (N-15 → 12) for 4 months each of three winters under controlled conditions (12 months of hibernation). All animals (with one accidental exception) were born in the laboratory, and each litter was divided between control and experimental groups. Each hibernator when in the cold showed bouts of deep hibernation for about 6 days at a time in the classic state of very reduced body temperature, heart-rate, breathing-rate and metabolism. The periodical awakening lasted about 12–24 hr. Observation methods and results have been detailed elsewhere[3,4]. During the second winter of hibernation one hibernator died and two others died during their usual summer stay in the warm room, which had heated up briefly to more than 32° C. due to a spell of hot weather. Since no control ground squirrels died of natural causes, we may speculate that for some ground squirrels hibernation may be directly or indirectly a stress. At the end of the hibernation period of the third winter, when the specimens were 3 years old, physiological measurements were made at room temperature on 12 hibernators and on the 14 control squirrels. Then both groups were killed, and a series of biochemical and morphological tests were made. At this time the squirrels should be considered at least middle-aged although the life-span of the thirteen-lined ground squirrel has not been determined. 13 of the series (5 hibernators and 8 non-hibernators) were examined histologically. The results were checked against 53 recently caught wild ground squirrels. The rest of this report will concern only the blood vessel findings in the histological observations. Some of the other results have been reported earlier[3,4].

Table 1. Distribution of Aortic Medial Calcification in Ground Squirrels raised in Laboratory (N = 13)

Aortic calcification	No calcification
Hibernators:	
Male*	Male (*a*)
	Female (*a*)
	Female
	Female
Non-hibernators:	
Female (*a*)†	Male
Male	Male (*b*)
Female	Female (*b*)
Female	Female

* More than four years old (trapped as adult); all others are three years old (born in laboratory).
† Letters, if present, identify litter mates.

Calcified plaques were observed in the media of the aorta in 5 ground squirrels (see Table 1). The lesions were histologically indistinguishable from human vascular medial calcification (also referred to as Mönckeberg's sclerosis or senile arteriosclerosis). The anatomical location, however, differed. In ground squirrels the lesion was found only in the proximal aorta (absent in the abdominal aorta and ileofemoral arteries) while the human lesion is more frequent and more severe in the larger muscular arteries of the extremities. The plaques were found in the inner three-quarters of the aortic media (Fig. 1). The largest plaques were two-thirds of the circumference of the aorta and three-quarters of the thickness of the aortic wall. Most plaques were sufficiently calcified to obscure all cytological detail in hæmatoxylin- and eosin-stained sections; after decalcification with hydrochloric acid, elastic lamellæ and smooth muscle cell nuclei were distinguishable in some, but others showed only amorphous debris. In some sections near the plaques there were many bluish, apparently calcific granules both along the elastic lamellæ and diffusely distributed in smooth muscle cytoplasm; also a few barely visible, bluish-staining granules (calcium ?) were found in the proximal aorta of 2 hibernators and the 1 non-hibernator all free of plaques. In some aortæ there was swelling and vacuolization of some smooth muscle cell cytoplasm, not consistently associated with calcification.

The findings in the laboratory animals were checked against the 53 wild ground squirrels. These were studied and dissected, and at least 50 per cent were determined to be more than one year of age. None

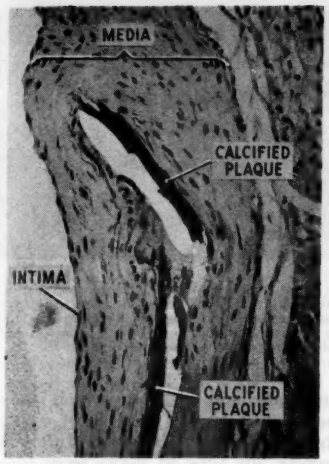

Fig. 1. Medial calcification in aorta of ground squirrel which did not hibernate during its life-span (three years). (× 110)

had aortic or ileofemoral arterial medial calcification. There was no atherosclerosis in any of the squirrels studied, wild or raised in the laboratory

Spontaneous aortic lesions like those in the ground squirrel have been described by Fox[5] in rabbits, cows, horses, wild canines, cats, marsupials and shore birds. It was not possible to determine from his account whether his material was more comparable to our laboratory series or to the field series. The lesions have also been produced experimentally by several methods, all relatively harsh[6]. Apparently diet did not produce the lesions in the present series since there was no evidence from a separate study of the teeth, weights and other indices, of any dietary abnormality in the laboratory squirrels. Spontaneous medial calcification increases with age in man[7,8], in the rabbit[9] and in the cow[5]. The same relationship would be expected in ground squirrels raised in an environment as nearly normal as laboratory conditions permit; yet none of the 3-year hibernating ground squirrels showed medial calcification (although found in 50 per cent of the controls). This evidence suggests that lowering metabolism (by hibernation) in some way reduces the occurrence of medial calcification in ground squirrels in the laboratory and probably also in the field environment of this local geographical area.

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Reduced Activity of Histaminase in Rats sensitized by *Bordetella pertussis*

SINCE Parfentjev and Goodline[1] published their work on histamine hypersensitivity induced by inoculation of *Bordetella pertussis* (reviewed by Kind[2]) a number of papers on the subject have appeared; but little has been reported of the related biochemical changes in connexion with susceptibility to histamine. Inactivation of histamine by lung tissues from mice inoculated with *B. pertussis* was reported by Kind *et al.*[3] to decrease as compared with tissues from uninoculated mice. But this interesting result was not repeated by the same authors. More recently, Fishel[4] has examined changes in amino-acids, histamine and glutathione contents in various organs from inoculated mice, revealing no specific changes referable to histamine hypersensitivity. The present communication deals with the results concerning reduced activities of histaminase in tissue of rats inoculated with *B. pertussis*.

Bordetella pertussis, phase 1, No. 18-323, was cultivated in a synthetic medium originally described by Kuwajima *et al.*[5] at 37° C. for 96 hr. The grown cells were centrifuged and the supernatant was incubated in the presence of 1/5,000 merthiolate at 37° C. for 48 hr. to detoxify lethal toxin. Male albino rats (Wistar strain) weighing 100–200 gm. were sensitized by a single intraperitoneal injection of 3 ml. of the supernatant. Tissues from the inoculated and the uninoculated rat were taken on the fifth day and homogenized in a glass homogenizer with 5 vol. of cold phosphate buffer (*p*H 7·4, *M*/15). A supernate obtained by centrifugation of the homogenate was dialysed against the same buffer at 4° C. for 20 hr. and assayed for histaminase by the method of Kapeller-Adler[6]. The standard assay system contained 5·5 ml. of the supernatant, 4·0 ml. of phosphate buffer (*p*H 7·4, *M*/15), 3·0 ml. of $1{\cdot}43 \times 10^{-3}$ *M* indigo disulphonate (Merck), 20 μgm. of flavine adenine dinucleotide and 3·0 ml. of $5{\cdot}5 \times 10^{-3}$ *M* histamine dihydrochloride or water. One drop of chloroform was added as a preservative. 2½ ml. of an aliquot taken at each incubation period was assayed in duplicate for histaminase activity.

Table 1. HISTAMINASE ACTIVITY OF LUNGS OF RATS SENSITIZED WITH *B. pertussis*

Normal	Sensitized
622*	257*
789	330
697	330
856	293
767	—
Mean 746 ± 112	330 ± 55·7

Statistically significant ($F_s = 85{\cdot}3 > F'_{(0{\cdot}01)} = 12{\cdot}25$).

* Histaminase activity: expressed as μgm. histamine degraded per gm. tissue, in 24 hr., at 37° C.

As shown in Table 1, the histaminase activity of sensitized rats was significantly reduced as compared with normal rats. In six subsequent experiments with 3 animals per group, a decrease in histaminase activity was again produced and examined statistically (ratio for decrease between the inoculated and the uninoculated rats is 59·5 ± 10·5 per cent for lung, 38·0 ± 14·3 per cent for liver). With tissues other than the lung and the liver, no definite histaminase activity was detected because the activity of such tissues was too low and because of the relatively higher blank titres. The decrease in histaminase observed can scarcely be ascribed to a general de-

pression of the metabolic activity, or to a shortage of prosthetic groups, because the inoculated animals were apparently healthy and enzymes other than histaminase, such as succino-oxidase or monoamine oxidase, showed no significant difference in their activities between the normal and the inoculated rat liver. The succino-oxidase activity was 274 and 296 µl. oxygen/100 mgm. tissue in 30 min. in the normal and the inoculated liver respectively. Monoamine oxidase was assayed with tyramine according to Creasy's method[7]. The uptake of oxygen was 237 and 220 µl./gm. tissue in 30 min. in the normal and the inoculated liver respectively. It is considered that reduced activities of histaminase may provide a clue to the explanation of histamine hypersensitivity in animals inoculated with *B. pertussis*.

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SINCE the work described above was carried out we have investigated the reduced inactivation of histamine by liver and brain from mice sensitized with *B. pertussis*. Histamine was added to a homogenate of the organs. Then the amount of histamine remaining after various intervals of incubation at 37° C. was determined by extracting histamine by a modified McIntire's method[1] and using guinea pig ileum. The extract responded to atropin and antihistamines in much the same way as histamine did. The liver and brain of sensitized mice showed a statistically significant reduction in the histamine-inactivating activity over non-sensitized mice.

The failure of reproduction of a reduced inactivation of histamine in mice sensitized with *B. pertussis*, as reported by Kind and Woods, may be due to their use of a more dilute homogenate than ours and a crude mixture instead of histamine extract.

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Secretion of Two Types of Saliva by an Aphid

NEARLY all phytophagous Hemiptera, including aphids, secrete a salivary material which coagulates rapidly on ejection to form a 'stylet-sheath' enclosing the path of the stylets in food materials and even in agar gel[1] and liquids[2]. It has been reported[3] that some Heteroptera secrete in addition a separate watery and water-soluble saliva which is emitted and sucked back both on the surface of substrates and within them. However, opinions differ on whether jassids secrete one type of saliva from which water-soluble substances diffuse before it gels[4] or two distinct types of saliva[5]; and among the Homoptera generally, only a sheath-forming secretion has hitherto been demonstrated conclusively.

Fig. 1. Photomicrographs of the stylet bundle (with food canal uppermost) and salivary secretions of *Aphis craccivora*. (*a*) Sheath material secreted on to the underlying glass slide; (*b*) the meniscus of a watery secretion which has been discharged from the salivary canal and sucked back into the previously empty food canal. Inset, sheath material being extruded from the tip of the stylet bundle

The salivary secretions of aphids are of particular interest since they can act as vehicles for many plant viruses and may also inhibit them[6]. Due to the smallness of the insects it is difficult to determine whether, during feeding, they emit any non-coagulating saliva in addition to the sheath-material; but the following observations indicate that *Aphis craccivora* Koch does in fact produce two types of salivary secretion.

The insects were cemented by the dorsum to a pinhead, anæsthetized with carbon dioxide, and secured so that the stylets, which were first slipped out of the rostrum, lay flat on a clean, dry glass surface. It was observed under the microscope that as soon as the insect became active again, the contents of the food-canal were suddenly sucked back, leaving the canal totally or partially filled with air. The mandibles would then begin to slide backwards and forwards over the maxillæ, and almost invariably a highly viscous secretion was discharged in a manner suggesting the extrusion of artists' oil paint from a tube. This secretion solidified almost immediately it left the stylets and was evidently sheath material. Occasionally, it was also possible to see sudden flushes of watery liquid issuing from the tip of the stylets, but the most convincing evidence that another secretion was produced was the sudden sucking back of liquid up the empty food-canal. The rapid movement of this liquid and its appearance at times when no sheath material was being discharged precluded the possibility that it was the latter secretion. Further, since no liquid passed down the food-canal, regurgitation of gut contents could not have occurred. It is evident, therefore, that *Aphis craccivora*, similarly to Heteroptera, secretes a watery saliva distinct from the material which forms the stylet-sheath.

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Bloat in Cattle

Much experimental work has been done on the causes of legume bloat in cattle and the prevention of its occurrence in the field (for reviews see Johns[1]). Several substances have been isolated from the feed or the animals' saliva, and have been reported to be responsible for the foam in the rumen of a bloated cow; but it has not been shown that any of these substances occur in the foam found in the rumen, and no attempt has been made to isolate the surface-active compound responsible for the foam directly from the rumen contents of a cow grazing clover or lucerne.

In my experiments, serial samples of rumen fluid were taken from cows through a permanent fistula, commencing before the beginning of either eating freshly cut clover and lucerne in the stall or grazing a new area and continuing for 6 hr. The *p*H, *e*H, total volatile fatty acid and ammonia nitrogen of the samples were determined. The remaining liquor was treated with 'Hyflo Supercel' to aggregate the suspended particles, and the straw-coloured filtrate was collected at the pump. The filtrate was found to foam considerably on shaking. The constituent responsible for the foam was not precipitable by mercuric chloride in the hot and was unaffected by a few minutes boiling with nitric acid or sodium hydroxide, but was decomposed by boiling for ½ hr. with 3 per cent nitric acid. It did not pass through a dialysis membrane. The foaming constituent was precipitated from solution by the addition of ethanol to a concentration of 70 per cent at *p*H 4. After centrifuging off, the ethanol precipitate was redissolved in water to give a solution which foamed on shaking, indicating that the compound was not denatured by the alcohol precipitation. These results suggested that the constituent was carbohydrate in nature. The ethanol-precipitated material was hydrolysed for 4 hr. with 3 per cent nitric acid free from nitrogen peroxide containing a crystal of urea and the neutralized hydrolysate chromatographed on filter paper. The main constituents were the sugars normally found in the pectin and hemicellulose fractions of plants.

In each of the three experiments it was found, by using an accurate empirical laboratory method, that maximum foaminess occurs in the rumen 1–2 hr. after the cow began eating clover or lucerne, and fell away 4 hr. later to the pre-feeding level; the rumen contents of these cows were more foamy at all times than the contents from any cow eating grass or winter rations. This observation suggested that the foaming constituent appeared in solution in the rumen liquor after the plant had been physically broken down, and that it later disappeared, probably by the degrading action of the micro-organisms.

The whole picture of the fermentation, in the rumen of a cow eating clover or lucerne, is of a rapid reaction, as indicated by the high volatile fatty acid and ammonia nitrogen concentrations with copious gas production, the latter being entrapped in small bubbles in the rumen liquor owing to the presence of the pectins and/or hemicelluloses. It is important to note that under these feeding conditions, both the requirements for foaming to occur, namely, high gas production and the presence of a surface-active agent, are satisfied together and bloating may therefore occur. Each factor occurring on its own in this or any other situation may have no detrimental effect on the animal. The postulation that plant pectins and hemicelluloses are the substances responsible for the formation of a foam in the rumen of bloating cows does not preclude absolutely that other factors may be involved.

I wish to thank Dr. G. S. Pope for assistance with the chemical tests on some samples of rumen liquor.

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PLANT PHYSIOLOGY

Effects of Auxins on Membrane Permeability and Pectic Substances in Bean Endocarp

It has been shown[1,2] that auxins delay the onset of senescence in bean endocarp and various leaf tissues (*Rhoeo*, *Mesembryanthemum*) maintained *in vitro*. In the absence of auxin, liquid-logging of intercellular spaces is followed by cellular dissociation and rounding off of cells. Similar changes have been observed in the abscission zones of *Coleus*, *Cestrum* and *Fuchsia*. When de-seeded bean pod segments are maintained in Petri dishes on wet filter paper, liquid-logging is evident in 2½–3 days and an exudate appears on the upper tissue surfaces. Cellular dissociation is usually complete by the fifth day. These changes are essentially prevented by the addition of an auxin (3-indoleacetic acid or α-naphthaleneacetic acid) to the culture medium. There are no significant differences in increase in fresh weight or respiratory activity between water- and auxin-treated endocarp segments over a ten-day period. The cells of liquid-logged segments are still capable of plasmolysis and deplasmolysis. The results indicate that the liquid-logging and exudation are manifestations of changes in permeability. A second process involves changes in the composition of the cell-wall cementing substances which take place in the absence of auxin and give rise to cellular dissociation and rounding off of cells.

Previous studies[3–6] have implicated pectin methylesterase as one of the enzymes directly affected by auxins. For pectin methylesterase, auxin appears to act through an adsorption–desorption mechanism which controls the activity of the enzyme in the tissue.

The results presented herein concern the nature of the permeability changes and the role of pectic enzymes in the processes causing cellular dissociation. Bean segments were prepared as before[2], and the exudate from water-treated segments collected for analysis. On addition of 3 vol. of ethanol, a precipitate was formed which was collected by centrifugation. The precipitate was dissolved in alkali, reprecipitated by acidification, and digested with a commercial pectinase preparation. The only substance detected in the digest was galacturonic acid. Analysis of ethanol-soluble substances in the exudate showed the presence of amino-acids, traces of organic acids and a large amount of a non-reducing sugar, which was identified as sucrose by paper chromatographic methods as well as identification of the hydrolytic products. Quantitative determination of the sucrose in the earliest-obtainable exudate gave a figure of 0·029 *M*. The osmotic pressure of the same exudate was found to be 0·050 *M*, thereby showing that sucrose is the major osmotic constituent. Ash

analyses indicated that inorganic ions contribute much of the osmotic pressure not accounted for by sucrose. Since the exudate is continuous with the liquid in the free space of the tissue, there are large amounts of solutes, including soluble pectic substances, in the walls of exuding segments. The presence of sucrose in the exudate indicates an increase in permeability as sucrose is not a hydrolytic product of wall polysaccharides.

The nature of the permeability changes was further investigated by measuring the apparent osmotic volume of the tissue with respect to sucrose, and relating these changes to the liquid-logging and exudation occurring in segments maintained in the absence of auxin. The apparent osmotic volume was measured by the method of Briggs *et al.*[7]. In this measurement permeability changes are indicated by a large decrease in the apparent osmotic volume of the tissue with respect to the solute used for the determination. The results for two different batches of beans show that the time at which the osmotic volume of water-treated segments commences to fall rapidly is correlated with the onset of liquid-logging and exudation, and that all these changes are markedly reduced or prevented by the addition of auxin to the medium.

The similarity of the microscopically observable sequence of events which occur in abscission zones of certain plants and in bean endocarp segments, coupled with the fact that auxin alters these events in a similar way, presented the opportunity to test a hypothesis[8] which purports to explain the auxin-controlled changes occurring in the cell-wall cementing substances of abscission zones. This hypothesis invoked the combined action of pectin methylesterase and endopolygalacturonase. The latter enzyme has been shown to act much more rapidly on de-esterified pectins, and an increased reaction-rate is therefore a natural consequence of the presence of an active esterase. It was proposed that the solubilization of pectic substances in abscission zones could be brought about by desorption (activation) of pectin methylesterase at low levels of auxin. If the hypothesis is correct and the auxin-controlled processes of abscission zones and bean endocarp are indeed analogous, it follows that pectin methylesterase should be present in the exudate from water-treated endocarp segments. Assays were carried out using a manometric technique described previously[5] and the presence of the enzyme in the exudate established. The actual amount of enzyme increased in an approximately linear manner over the 4-day period.

In further support of the above hypothesis explaining solubilization of pectic substances, evidence has been obtained for the presence of a polygalacturonase-like enzyme capable of reducing the molecular size of pectic acid. The occurrence of this enzyme has been reported only in a few instances in higher plants (tomato[9], avocado[10], pear[11]). Viscosity measurements were carried out on pectic acid solutions using either tissue slices or a cell-free extract as the enzyme source and with appropriate controls. Significant reductions in viscosity were measured in both cases.

These results show that a low level of auxin in bean endocarp gives rise to permeability changes and to alterations in pectin metabolism which are correlated with liquid-logging, surface exudation and cellular dissociation. The results suggest that the action of auxin may be a surface phenomenon affecting the physico-chemical characteristics of cellular membranes and interfaces as previously proposed by Veldstra and Booij[12]. Two of the manifestations of this effect would be changes in membrane permeability and changes in the amount of pectin methylesterase adsorbed at cellular interfaces. Full details of this work will be published elsewhere.

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Carbohydrate Constituents of the Mycelium of *Penicillium chrysogenum* grown in Media with Different Sources of Carbon

There are several reports on the carbohydrate constituents of the mycelium of different strains of *Penicillium chrysogenum* grown under different conditions. The presence of mannitol, erythritol, a polysaccharide containing glucose, mannose and galactose[1], pentosan[2], phosphates of mannose, and inositol[3] and of glucose, fructose, pentose and heptose[4] have been reported. Shu and Thorn[5] grew *P. chrysogenum* Q176 in Czapek–Dox medium with 5 per cent glucose, galactose and xylose individually as the sole carbon source and reported that the mycelial hydrolysate in each case consisted of glucose.

We have grown *P. chrysogenum* (strains *HA*-6 and *HA*-9, used in production here) in shake flasks in the synthetic medium of Gitterman and Knight[6] with 2 per cent sucrose, lactose, glucose, galactose, fructose, L-sorbose, mannitol, *myo*-inositol, *myo*-inosose-2, glucuronolactone, ribose, xylose, L-arabinose, glycerol and sodium acetate as the sole carbon sources. The inoculum was the centrifuged and resuspended 'seed mycelium' (used for inoculating the big fermentors) grown in the 'seed tanks' of the plant in corn-steep–sucrose medium with aeration and agitation for 48 hr. after inoculation with spores. When the carbohydrate in the medium was almost exhausted (3–8 days), the cells were collected, washed with water and dried. In addition, three samples of 'seed mycelia' (S_1, S_2, S_3) and three samples collected from the fermentors (*F*-1374, *F*-2380 and *F*-2382) at the end of fermentation (98–110 hr.) were also taken up for comparative study.

The dry, well-powdered mycelium (100 mgm.) was extracted three times with ether, three times with *iso*propyl alcohol (which removed mannitol), and then three times with cold water to give a total of 10 ml. of the cold-water extract (*A*). The residual mycelium was treated with 1 ml. of 80 per cent

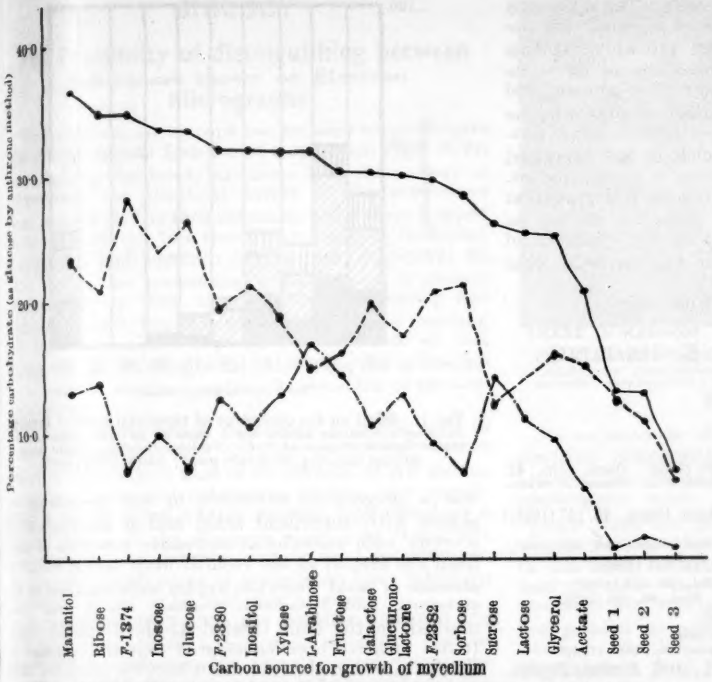

Fig. 1. The carbohydrate content of the aqueous extract (*A*), the polysaccharide (*B*), and total carbohydrate (*A* + *B*) as estimated by anthrone method and expressed in terms of glucose. The samples are arranged in the descending order of total carbohydrate content.
–·–, *A*; – – – –, *B*; ———, *A* + *B*

sulphuric acid, allowed to stand for about 2 hr. for solution and then diluted to 10 ml. The insoluble material (probably chitin) which separated was filtered off, and the filtrate (*B*) heated on a boiling water-bath for 3 hr. to give the hydrolysate (*C*). The carbohydrate content of (*A*) was assayed by the anthrone[7], Somogyi[8] and periodate[9] methods (to detect the relative amounts of polysaccharides, reducing sugars and sugar alcohols), of (*B*) by the anthrone method (to estimate the polysaccharides) and of (*C*) by the Somogyi method. The results obtained are presented graphically in Fig. 1.

The aqueous extracts and neutralized hydrolysates were passed through 'Dowex 50' (H^+) and analysed for sugars by the spectra with unsulphonated and presulphonated resorcinol according to the method of Devor, Conger and Gill[10] and by descending paper chromatography on Whatman No. 1 paper, using 80 per cent *iso*propyl alcohol as the solvent and silver nitrate, aniline phthalate and phloroglucinol as dip reagents. For confirmation, water eluates of the paper strips cut out from the chromatogram corresponding to the various spots were analysed by the resorcinol spectra[10]. The results obtained and the points of interest that emerge from these studies are as follows:

(1) *Total carbohydrates* (*A* + *B*). This varies from 20·6 to 36·5 per cent, depending upon the nature of the sugar used, with no correlation being apparent between this percentage and the structure of the sugars.

(2) *Water extract* (*A*). This accounts for 20–52 per cent of the total carbohydrates in the various samples. The component sugars seem to be almost the same in all the samples, though there are quantitative differences. Glucose accounted for about 90 per cent of the total, probably with traces of galactose. Chromatography revealed five more carbohydrates—ribose, three disaccharides giving glucose on hydrolysis, one of which is most probably trehalose, and one with R_G 140 which does not appear to be glucuronolactone.

(3) *Hydrolysates* (*C*). All the samples were found to consist of the same sugars. Glucose was again the predominant sugar with perhaps traces of galactose. In addition, there were a sugar with R_G 50 which is not inositol, the compound with R_G 140, and a compound with R_G 110 which is not fructose or sedoheptulose and gives a complex resorcinol spectrum. Ribose was not detected. There is an inverse correlation between the percentage of the sugar content in the aqueous extract (*A*) and the hydrolysate (*C*), the significance of which is not clear at the moment.

(4) *Seed Mycelia*. These stand out as a class by themselves. The total carbohydrate content and also the percentage of the sugar in the aqueous extracts are low. The aqueous extract consisted of fructose, ribose, a small quantity of glucose, traces of trehalose and the sugar with R_G 140. On hydrolysis of this aqueous extract with *N* sulphuric acid for 30 min., the sugar content apparently increased two- to three-fold, and galactose appeared as the predominant sugar in the hydrolysate. The hydrolysate of the water-extracted residual mycelium was found to be of the same pattern as the hydrolysates (*C*) of the other mycelia, except that ribose was also detected here.

P. chrysogenum can utilize a variety of sugars and carbon sources for growth, though the degree of growth varies. It is striking that, irrespective of the nature of the sugar or the carbon source used in the medium, the component sugars in the aqueous extract (*A*) and the hydrolysate (*C*) remain the same, glucose being most predominant. There exists, therefore, a mechanism for the conversion of all the sugars and carbon sources first into glucose, which afterwards becomes converted into the polysaccharide. To elucidate these metabolic pathways, we are analysing the culture fluids for intermediates in the growth experiments with the various sugars. The concentration of sugars in the 'free sugar pool' of the aqueous extract would be the resultant of the quantity of the sugars synthesized from the media component and the drain by the conversion into the polysaccharides. It could be expected that, when the rate of growth of the mycelium is low with little demand from the 'free sugar pool', there would be an accumulation of these sugars in the pool and vice versa. The latter situation seems to be prevailing

in the fast multiplying seed mycelia. The difference we have noticed between the 'seed mycelia' and the full-grown one in the fermentors probably explains why the former produces no penicillin at all while the latter does[11]. The presence of free glucose and ribose and also the large percentage of sugars in the 'free sugar pool' of the aqueous extracts is of interest. Whether the sugars exist as such or are produced during the processes of extraction is being studied. The free ribose detected need not be a degradation product of nucleic acids, but could be the excess produced over what is diverted for the synthesis of the nucleotides and also used up for conversion into glucose.

Full details will be published elsewhere.

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Control of Superficial Scald in Stored Apples

Although superficial scald of apples is effectively controlled by wrapping in paper impregnated with mineral oil the labour involved in doing so renders the method expensive, and the search for alternative methods of control continues. Fidler[1] has shown that the view that superficial scald is attributable to an injury to the tissues caused by volatile products of the metabolism of the fruit fails to explain many of the observed phenomena. He has suggested that an interaction between a heavy volatile substance *Y* which cannot be removed from proximity to the fruit by ventilation and a non-volatile substance *X* produces a compound or compounds toxic to the skin. Recent observations made during the course of experiments on the control of low-temperature injury would seem to support Fidler's view.

Apples of the variety Bramley's Seedling were picked from twelve large trees at three different dates. Comparable samples were made up within each harvest and were stored on trays in air at 0° C. Four trays from each harvest were placed at 15·5° C. for 5 days commencing with the date of picking and afterwards at intervals until the thirtieth week. Up to the twelfth week the warming was applied at fortnightly intervals. No tray of fruit was subjected to warming more than once.

Fig. 1 shows the percentage of fruits affected in the second harvest after 34 weeks from the date of storing. The relationship shown is characteristic also of that obtained with the two other harvests, although the amount of scald in the last pick was small, as is usual with fruit of more advanced maturity. There

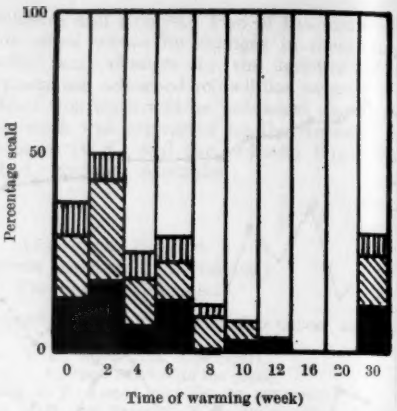

Fig. 1. Effect on the occurrence of superficial scald of keeping Bramley's Seedling apples for 5 days at 15·5° C. at successive stages during storage at 0° C. Vertical hatching, slight scald; oblique hatching, moderate scald; black, severe scald

was a progressive reduction in the percentage of apples with superficial scald and a diminution of severity with warming at successive intervals of time from the second to the twelfth week and a complete absence of scald when the apples were warmed at the sixteenth and twentieth weeks. Scald was very marked on the fruit treated at the thirtieth week. It has hitherto been considered that the damage to the fruit, although it does not become manifest until later, is incurred before the sixth–eighth week after putting into store[2]. These results suggest that this is not necessarily so.

Kidd and West[3] observed that very brief intermittent warming of Newton Wonder apples during storage at 3° C. reduced the amount of scald. Treatment, however, commenced early in the storage life and was continued throughout the period.

A possible explanation of the result described above is that the combination of substances *X* and *Y* is cumulative and reversible at higher temperatures, so that when warming is carried out prior either to the build-up of a sufficient concentration of the toxic substance or before the substance has had time to react lethally upon the cells, no scald injury results. If, however, the time-interval exceeds a certain limit, scald will appear in an amount increasing with extension beyond this limit. Although in Fig. 1 no observations are recorded for warming at intervals between the twentieth and thirtieth week, it can safely be assumed that, had they been made, an upward gradation in the amount of scald would have appeared in this interval.

From the practical point of view change of temperature would seem to be a possible method for control of superficial scald provided the fruit could be stored at 0° C. without low-temperature injury or provided the same effect could be secured at a temperature of storage above the critical level for low-temperature injury.

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BIOLOGY

The Possibility of distinguishing between Substances shown on Electron Micrographs

THE electron microscope can be used to investigate the morphological features of a specimen right down to the molecular level, but there is as yet no way of identifying the chemical nature of the substances seen, except on the rare occasions when these happen to be crystalline. In a specimen of uniform thickness, a region of high electron opacity may, in general, be said to be one containing substances of a greater weight density than those of the surrounding less opaque region[1], but this gives little help in deciding on their chemical composition. The lack of any direct way of knowing what substances one is looking at is perhaps the most serious shortcoming of electron microscopy.

It thus seems worth describing a simple way in which the image formed by an element of high atomic number differs from that of an element of low atomic number. Biological substances seldom vary significantly in the mean atomic number (calculated on a weight basis) of the elements composing them, but the method to be described can be used, for example, to identify which parts of a specimen have taken up an added 'stain' of high atomic number.

It is well known that the contrast between the different features of a biological specimen can be increased by reducing the size of the objective-lens aperture. This observation is in good accord with the theory of electron scattering deduced from considerations of quantum mechanics[2,3]. Hall and Inoue[4], for example, found that when the angular aperture of the objective was reduced from $4{\cdot}2 \times 10^{-3}$ to $2{\cdot}1 \times 10^{-3}$ radian, the scattering cross-section of polystyrene latex increased by 30 per cent. Lenz's theory[2,3] predicts an increase of about 25 per cent. But with an element of high atomic number, theory suggests that the size of the aperture will have little effect on contrast. I have made observations which in fact confirm this; for, unlike carbon, films of gold, platinum and tungsten show no detectable change in opacity when the objective aperture is changed for one of half the size.

The method of differentiating substances of high atomic number from biological or other material of low atomic number thus consists simply of taking two electron micrographs of the same field using a different-sized aperture for each. With many microscopes, changing the aperture involves only a simple manipulation that does not even require the beam to be switched off. The two plates are similarly exposed and developed. All substances with a mean atomic number (Z) less than 12 should show an image of markedly different density on the two plates. Two conditions, however, must be satisfied for this change to be seen. First, the image of any object under test must be considerably less dense than the background of supporting film (that is, the object must have a sufficient electron opacity): secondly, the plates must be exposed for long enough to give this image an optical density of about 0·5 or more (that is, distinctly darker than an unexposed part of the plate). If these conditions have been satisfied, then an object showing no change in opacity may be safely identified as one containing a large content of material with an atomic number greater than 20.

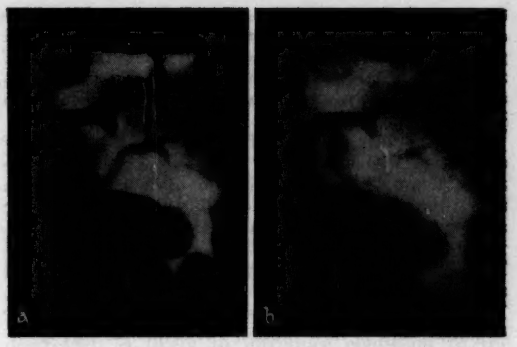

Fig. 1. Electron micrographs of polystyrene latex spheres surrounded by phosphotungstic acid (× 45,000); (*a*) using an objective aperture of 10^{-2} radian; (*b*) using an objective aperture of 5×10^{-3} radian

As an example of the method, Fig. 1*a* shows an electron micrograph of some polystyrene latex spheres surrounded by a dried-down mass of phosphotungstic acid. The latex spheres were less opaque than the phosphotungstic acid and can be clearly distinguished. A second plate was exposed of this same field but using an objective aperture of half the size. The plate was reproduced in exactly the same way and is shown in Fig. 1*b*. (Both figures are printed as negatives, that is, as the original plates.) The latex particles are now almost indistinguishable from the surrounding material, the polystyrene latex (mean $Z = 5{\cdot}6$) having gained considerably in opacity while the phosphotungstic acid (mean $Z = 58$) did not. The demonstration is made more vivid if the plate shown in Fig. 1*a* is projected in red light and the image superimposed on that of Fig. 1*b* projected in green light. The objects of low atomic number then appear green against the material of high atomic number, which looks yellow.

A full mathematical treatment of this topic will be given elsewhere, but it seems that a quantitative application of the method would allow one to differentiate calcium ($Z = 20$) or even phosphorus ($Z = 15$) from, say, protein (mean $Z = 7$). It would not, however, be possible to distinguish between the chief biological materials, proteins, carbohydrates, lipids and nucleic acids in this way, or to distinguish between any of the higher elements ($Z > 25$).

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Enzymic Hydrolysis of Fucoidin by *Pseudomonas atlantica* and *Pseudomonas carrageenovora*

FUCOIDIN, a common polysaccharide sulphate in brown seaweeds, has been shown by methylation[1,2] and acetolysis[3] to consist of a chain of L-fucopyranose units joined in α-glycosidic linkages through carbon atoms 1 and 2 of adjacent units, each unit being sulphated on carbon atom 4. The results obtained

from methylation studies also indicate that 1 : 3 and 1 : 4 linkages are present. A fucoidinase would greatly assist further studies on the structure of fucoidin. The object of this communication is to report the discovery of such an enzyme obtainable from two species of marine bacteria.

Fucoidin was prepared from *Fucus vesiculosus* by extraction with hot water[4]. Bacterial cultures were taken from a private collection of marine bacteria which had been used for degradative studies of agar and carrageenin. They had been isolated from seawater and marine algae in the neighbourhood of Halifax, Nova Scotia. *Pseudomonas atlantica*[5] hydrolysed agar and a Gram-negative rod hydrolysed carrageenin[6]. The latter was afterwards shown to have a polar flagellum and is now named *Pseudomonas carrageenovora* n.sp.

The micro-organisms were grown for 72 hr. at 20° C. on a rotary shaker in a medium which contained sodium chloride, 30·0 gm.; dipotassium hydrogen phosphate, 1·0 gm.; crystalline magnesium sulphate, 0·5 gm.; sodium nitrate, 0·5 gm.; ferric chloride (1 ml. of a 2·0 per cent solution); fucoidin, 2·5 gm./l. of distilled water.

The utilization of fucoidin by the marine bacteria was determined from the fucose equivalents of aliquots removed from the control and fermentation flasks. The fucose equivalent of fucoidin was obtained by hydrolysing an aliquot of the medium with 0·5 *N* hydrochloric acid in a sealed tube for 18 hr. in a steam-bath. The hydrolysate was cooled, neutralized and the concentration of fucose determined by the method of Somogyi[7] with fucose as standard. The amount of fucoidin utilized by *P. atlantica* was 31·5 per cent and by *P. carrageenovora* 29·9 per cent.

The cell-free medium was used as the enzyme solution. One volume of enzyme solution was added to two volumes of 0·9 per cent solution of fucoidin in 0·2 molar phosphate buffer. Aliquots were removed at intervals, and the increase in reducing power, expressed as fucose, was determined by Somogyi's method[7].

The relationship between *p*H and enzyme activity is shown in Fig. 1. The enzyme activity was greatest around *p*H 7·0. After 24 hr. at 40° C. and *p*H 7·0 the

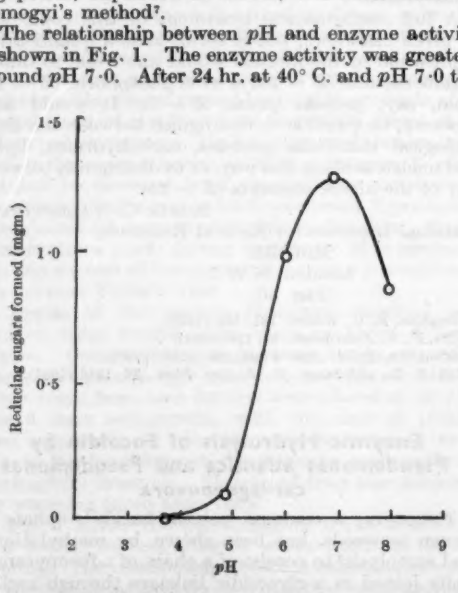

Fig. 1. The relationship between pH and enzyme activity. Reducing sugar as fucose after 3 hr. at 40° C. Enzyme solution from *Pseudomonas atlantica*

Table 1. Enzymic Hydrolysis of Fucoidin

Enzyme from	Fucose (mgm.)		Hydrolysis of fucoidin (per cent)	
	3 hr.	24 hr.	3 hr.	24 hr.
P. atlantica	1·07	2·10	12·3	24·2
P. carrageenovora	1·19	1·39	13·7	15·9
*P. atlantica**	—	0·81	—	8·9

* Enzyme solution heated for 10 min. at 100° C.

apparent degree of conversion of fucoidin to fucose by enzmye preparations from *P. atlantica* and *P. carrageenovora*, was respectively 24·2 per cent and 15·9 per cent (Table 1).

The enzyme solution was heated for 10 min. at 100° C. and then added to the fucoidin. Results in Table 1 show an 8·1 per cent hydrolysis of fucoidin in the cell-free mixture. A similar effect was noted in previous experiments with a *K*-carrageenase. Further studies are planned on the purification of the enzyme and identification of the hydrolytic products.

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Marlins in British East African Waters

The first confirmed report of the striped marlin (*Makaira audax*) in the Indian Ocean was that of Smith[1], who recorded details of a 160-lb. specimen of 89 in. (2,260 mm.) standard length from Mossel Bay, South Africa. Morrow[2] reported having seen the striped marlin off Pemba Island and Mombasa in 1950; but no specimens were caught or examined. Copley[3] records a so-called striped marlin taken by him off Mombasa in 1934 (weight, 127 lb.) but does not mention the striped marlin at all in his "Game Fishes of Africa"[4].

I agree with Smith[1,5] that the name *M. audax* Phillipi 1887 for the striped marlin has priority over *M. mitsukurii* (Jordan and Synder) 1901 used by LaMonte[6] and most American workers prior to that publication. LaMonte hoped that a change in the law of priority under "The Rules" would allow *M. mitsukurii* to stand, but this was not so. *M. audax* has been used by later American workers, such as Royce[7] in his paper on the Central Pacific spearfishes, although Morrow[8] still retains the name *M. mitsukurii* in discussing races of the striped marlin in the Pacific.

During recent cruises of the *Manihine* (the research vessel of the East African Marine Fisheries Research Organization) during October–December 1958, a deep long-line was used for the capture of yellow-fin tuna (*N. macropterus*) and among the catch were 15 striped marlin—a further seven were lost while hauling. Catches were made between Malindi, Kenya (3° 20′ S.), and Mafia Island, Tanganyika Territory

Table 1. Length and Weight of *M. audax* in East African Waters

	1954	1958													
Total length (mm.)	2,590	2,200	2,530	2,485	2,515	2,580	2,480	2,700	2,590	2,770	2,560	2,650	2,800	2,735	2,760	2,830
Standard length (mm.)	2,250	1,860	2,150	2,185	2,160	2,210	2,125	2,300	2,250	2,325	2,180	2,360	2,510	2,360	2,450	2,395
Weight (lb.)	115	75	105	115	120	127	130	130	135	145	148	150	160	165	185	190

(8° S.), 10–20 miles offshore. It would seem, therefore, that striped marlin are not so rare in these waters, at least during the last three months of the year, as records, or the lack of them, would suggest. A marlin taken by trolling on October 5, 1954 (at 7° 35′ S., 39° 54′ E.), and recorded in the annual report of this Organization for 1955–56 [9], as *Tetapterus brevistoris* Playfair was, from the details, undoubtedly a striped marlin. In Table 1, total and standard length in mm. and weight in lb. are given for East African specimens of *M. audax* taken so far.

Certain proportions for the East African specimens are compared with those for LaMonte's Pacific specimens and that of Smith from South Africa in Table 2.

Table 2. Comparison of *M. audax* from the Pacific Ocean and South and East African Waters

	LaMonte Pacific specimens. Range	Smith South African specimen	East African specimens. Range
Head in standard length	2·46–2·72	2·61	2·64–3·02
Depth in standard length	5·4–6·58	6·59	5·70–7·03
Depth in pectoral length	1·0–1·8	1·53	1·16–1·43
Height of dorsal lobe in depth	= or less than 1	0·75	0·78–0·97
Height of dorsal lobe in pectoral length	1–1·3	1·15	1·04–1·34

East African striped marlin are brilliantly coloured—cobalt blue above and white below on the belly; the number of pale lavender coloured stripes varies considerably. On death, the fish becomes a uniform slate-grey above and pale below; the pale stripes persist after death for some time, but after refrigeration for a few days the stripes may be lost altogether.

It is interesting to note that no other species of marlin has been taken by this Organization (1951–to date) or seen by us in the fish markets of East Africa. It seems probable, however, that the black marlin is also present in these waters, although the records are somewhat dubious. Morrow[2] records a black marlin (*M. nigricans marlina*) from Pemba of 259 lb. and 2,151 mm. standard length, although Smith[5] points out that this is approximately 100 lb. greater than the average weight at that length. Similarly, Copley[10] records a so-called black marlin taken off the Kenya coast of 360 lb. at 3,365 mm. standard length, considerably less than the average for a black marlin of that size. *Histiophorus brevistoris* Playfair, said by Smith[5] to be the black marlin, is, I think, to be more correctly treated as *species indeterminata*, as did LaMonte[6], although Playfair's fish does possess more features like the black marlin than the striped. Playfair's type from Zanzibar was destroyed; the only species of marlin seen in Zanzibar markets in the past eight years has been *M. audax*.

Further details on the biology of the striped marlin will be given at a later date when the whole problem of long-lining off the East African coast will be discussed.

I must point out that *Marlina jauffreti* Smith 1956 [8], from Mauritius, was named purely on the details of a marlin visible in a not very clear photograph and a few notes received by Smith. Although a new species of marlin may be present in Mauritius waters, the establishing of a new species of fish on the basis of a photograph and without access to the fish itself at a later date (it appears to have been destroyed) is likely to introduce confusion to the system of nomenclature and is to be deprecated, especially in such a closely related group as the marlins.

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Development of Ovarial Teratomas in Viviparous Toothcarps by Pathological Parthenogenesis

Recently, I described three cases of pathological parthenogenesis in viviparous toothcarps, in which the stimulus required for the development of the unfertilized oocytes consisted in a local infection with the *Ichthyophonus* parasite, the phycomycete *Ichthyophonus hoferi* Plehn-Mulsow[1].

As some years ago I had observed in a *Lebistes* female an ovarial teratoma which also showed a close relation with an *Ichthyophonus* process[2,3], I was under the impression that teratomas can develop parthenogenetically in the viviparous toothcarps as well. I therefore decided to continue the systematic examination of the virgin females, hoping in this way to make some contribution toward explaining the origin of teratomas in general.

In this investigation one ovarial teratoma was observed on 1,484 adult virgin females of *Lebistes reticulatus* as well as on 1,179 adult virgin females of *Xiphophorus maculatus*, whereas on 946 adult virgin females of *Xiphophorus helleri* no ovarial teratoma was present.

The *Lebistes* teratoma, which was present in a 41-mm. female, was composed of connective tissue, musculature, cartilage, bone, blood vessels and nervous tissue, whereas in the *Xiphophorus* teratoma, occurring in a 68-mm. female, also intestinal structures, glandular structures and cysts could be demonstrated.

In both cases an *Ichthyophonus* process was present in the ovaries and in their surroundings, of which the

cysts varied in size and were localized in the cranial part as well as in the caudal part of the organ.

For microscopic confirmation of the virginity of the fishes, the sperm chambers of the ovaries were examined; no spermia were found. On the strength of this finding, self-fertilization—a phenomenon accidentally occurring in the viviparous toothcarps and explained by the presence of a bisexual gonad producing spermia and oocytes—could be excluded.

The coincidence of the ovarian teratoma on one hand, and the occurrence of the *Ichthyophonus* infection on the other, justifies the assumption that the development of a tumour is caused by the *Ichthyophonus* toxin, which provided the artificial stimulus for the parthenogenetic development of an unfertilized oocyte to teratoma. In this case the pathological process resulted in the parthenogenetic development.

It is not known why, in the cases formerly described, the local *Ichthyophonus* process caused a parthenogenetical development of the unfertilized oocytes and in other cases a pathological development to teratoma. In the latter cases, the damage to the unfertilized oocytes by the agent causing inflammation may have been such that normal embryological development was no longer possible.

It may be remarked that Spurway[4] did not mention the occurrence of teratomas in the virgin *Lebistes* females.

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Ultrastructure of Pineal Eye Sensory Cells

Work on the ultrastructure of photoreceptor elements in the lateral eyes of vertebrates[1–3] has advanced to the extent of becoming incorporated in a recent edition of a well-known text-book[4]. Ultrastructural research is also being done on invertebrate compound eyes[5,6]. So far as could be ascertained no work has yet been published on the ultrastructure of the eye-like pineal structures occurring in several vertebrate classes. For various reasons, such as compactness of pineal epithelia[7], small size of the structures involved[8] and bad preservation arising from fixation difficulties[9], there is considerable divergence of opinion and uncertainty regarding the nature and structure of the pineal sensory cells and their appendages as seen with the light microscope.

I have examined the ultrastructure of the inner and outer segments of the sensory cells in the adult pineal eye of the lizard *Cordylus polyzonus*. The structure of the appendages in this species has already been studied with the light microscope[10].

The material for the present study was fixed for 2 hr. in 1 per cent osmic acid buffered to pH 7·5 (veronal acetate) at 2° C. The fixation procedure previously employed[10] which involved injection of fixatives into, and their drainage from, the subdural cavity was abandoned in favour of, after paraldehyde anæsthesia, simply cutting out a flap of cranial roof containing the pineal eye and immersing this material in the fixative. This method, ensuring proper penetration, gave superior structural preservation. The material was embedded in *n*-butyl methacrylate, sectioned with a Porter–Blum ultramicrotome and studied under a Siemens electron microscope.

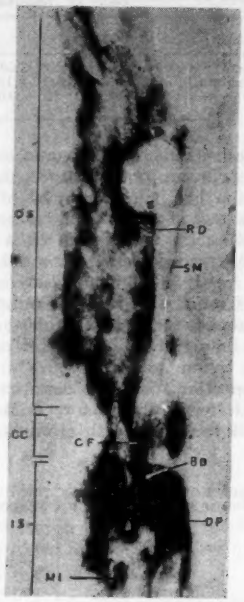

Fig. 1. Electron micrograph showing parts of the inner and outer segments of a sensory cell from the pineal eye of *Cordylus polyzonus*. The microstructure of these segments appears to be completely identical with that of the corresponding elements in the lateral eye. *BB*, basal body; *CC*, connecting cilium; *CF*, ciliary fibril; *DP*, dense particles; *IS*, inner segment of sensory cell; *MI*, mitochondria; *OS*, outer segment of sensory cell; *RD*, rod disks; *SM*, surface membrane. (× 16,000)

The results obtained indicate that, among possibly more than one type of sensory cell in the pineal eye, there are sensory cells with inner and outer segments almost completely comparable in structure to the same elements in the vertebrate lateral eye. Thus the inner segment (projecting into the pineal eye lumen) contains mitochondria, dense particles and a basal body in which a connecting cilium terminates. This latter connects the inner segment to the outer segment, and is composed of a so far unknown number of ciliary fibrils, no cross-sections through the connecting cilium being available yet. Some of these ciliary fibrils show up clearly, however, in Fig. 1, illustrating a longitudinal section through part of a sensory cell. In the outer segment the surface membrane and so-called rod disks are clearly recognizable, and appear to be identical with their counterparts in the rods of the vertebrate lateral eye. In view of the great similarity in the structure of the photoreceptory cells wherever they occur in the animal kingdom (that is, in lateral eyes of vertebrates, in the compound eyes of insects and arachnids), the conclusion would seem to be justified that the cells of the pineal eye possessing a microstructure of the same type are actually photoreceptory cells. Further investigations on this subject are in progress.

I should like to record my appreciation of the interest shown in this work by Prof. B. I. Balinsky, who gave me facilities for this work, and to thank Miss A. de Kock and Mr. J. W. Matthews for skilled

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Delayed Denervation and Accessory Limb Formation in Urodeles

FROG kidney adenocarcinoma implants and normal adult frog kidney implants made subcutaneously on the dorsal radioulnar surface of non-regenerating larval salamander forelimbs cause the host limbs to respond to their presence by forming supernumerary hand-wrist structures. Larval host limbs may on occasion fail to elicit any morphological response[1]. On the other hand, adult salamander host limbs may form: (*a*) an accessory structure comparable with the larval response; (*b*) nothing; (*c*) single or clustered subcutaneous cartilaginous nodules as in Fig. 1[2,3]. Although these nodules are commonly found in adult host limbs, they had never been produced by larvæ in hundreds of cases assayed.

Serial denervation of larval host limbs, by resection of brachial plexi, begun at 4 days post-implantation, will prevent the production of supernumerary structures[4]. The necessity of innervation for amphibian limb regeneration is well known[5], and in this case the trauma of foreign implant material did not act as a substitute for the influence of the nerve.

The experiments reported here entail denervations of brachial plexi of host limbs, which were delayed 12, 13, 14, 16 and 19 days post-cancer implantation, in 14 larval *Taricha granulosa* and 15 larval *Amblystoma opacum*. The technique has been reported previously in detail[4]. No supernumeraries were recovered in the 12-, 13- and 14-day groups, although three were obtained from the 16- and 19-day groups. The significance of the results is not simply that delayed denervation effects supernumerary development but is in the fact that 5 cases of cartilage nodule formation were obtained in these larval limbs.

These results with the larvæ suggest some ideas regarding this process. They indicate that delayed withdrawal of innervation may be tantamount to removing the growth stimulus to the blastemal mesenchymal cells, cells which are chondrogenically oriented with respect to their developmental potential[6] and, as a consequence of withdrawal of the growth stimulus, these aggregations differentiate into cartilaginous nodules. The common occurrence of nodules in adult host limbs might similarly be explained by co-ordinating certain assumptions and

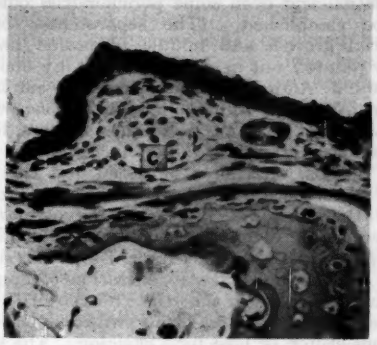

Fig. 1. Longitudinal section of an adult *Triturus viridescens* host limb bearing a subcutaneous accessory cartilage nodule *c*, which was induced to form by a frog kidney adenocarcinoma implant. (× *c.* 120)

experimental facts to bring about 'theoretical delayed denervations'. The assumptions represent equal and opposite alternatives, and are as follows: (*a*) the terminal innervation pattern of adult urodele limbs may be reduced from the larval condition; a possible extrapolation of the results of Van Stone[7,8], or (*b*) the terminal innervation threshold necessary to support regeneration may be higher in adult than larval limbs, see Singer[5]. Each would have the effect of making it more difficult to obtain innervation sufficient to support accessory morphogenesis in adult host limbs.

Although implant trauma may aid in bringing about dissociation of soft mesodermal host limb tissues to establish a mesenchymal population, these cells will only undergo accumulation into a blastema under the influence of innervation. If the innervation continues to be adequate to support growth and morphogenesis, then a supernumerary will result. If, however, it becomes reduced, subsequent to accumulation and some growth, nodule formation will be obtained.

How, then, can we account for this type of neural reduction in adult host limbs? It seems likely that the implant-induced situation may share with the amputated regenerating limb the possession of a temporarily increased terminal nerve supply[5], and in adult host limbs we have two factors which could combine to bring about a premature return to the normal adult-level. First of all, we know that due to an increased foreign body response in adult Amphibia, the implant will be destroyed more rapidly in adult limbs than in larvæ. Secondly, we know that blastemal formative processes, and indeed all morphogenetic processes, of adult limbs are considerably slower than these same processes during larval limb regeneration. Thus the combination of a more rapid disappearance or at least reduction of the traumatic stimulus and slower blastemal and morphogenetic events could easily account for a premature return to normal innervation patterns with nodules, rather than a supernumerary, the more usual end result.

Previously, I referred to the dissociation of soft, mesodermal tissues of the host limb to provide cells for the future blastema. This statement should be clarified by pointing out that it is usual in implant-induced accessory limb formation that the skeleton of the supernumerary does not articulate with or grow out from the 'mother' limb skeleton. If, however, the traumatic influence bringing about the dissociation of host tissues reaches the skeletal region, then

articulation and even some perichondrial outgrowth will be established. (The separateness of perichondrial growth and nodule formation has been clearly pointed out in an experiment by one of my students, J. Andrew Armer. Deviated, cut brachial nerves of the upper forearm of adult *Taricha granulosa* are capable of inducing, in distinct fashion, humeral perichondrial growth *and* nodule formation in soft tissue regions. It should be noted, lest this appear to be contradictory to the thesis of the preceding, that in these instances little or no nerve *growth* could be discerned by silver stain techniques, indicating low-level innervation.) The implant-induced situation might be likened to the regeneration of amputated dehumerized limbs in that the skeleton of the accessory structure usually forms without the aid of *adjacent stump or host limb skeleton.* The nodules, which now may be considered as having been formed as the result of abortive attempts at supernumerary formation, follow the same pattern in the sense that they appear anatomically separated from the 'mother' *limb skeleton.*

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Induction of Subcutaneous Nodules in Rabbits with the SE Polyoma Virus

The *SE* polyoma virus grown in mouse embryo cell cultures is capable of inducing a wide spectrum of histologically different neoplasms in hybrid $(C_3Hf \times AKR)F_1$ [1] and randomly bred Swiss mice[2], and sarcomas and angiomatous lesions in hamsters[3], and rats[4], if injections are made when the animals are new-born. Tumours in these animals increase in size and number and eventually kill the animals. Contrary to experience with these rodents, new-born rabbits of mongrel breed reacted by developing multiple subcutaneous nodules that later regressed.

The virus was propagated in mouse embryo cell cultures maintained with synthetic medium 199 [5] containing 2 per cent horse serum heated to 56° C. for 30 min. The medium was replaced at weekly intervals and only fluid from cultures incubated with the virus for 14 or more days was used for transferring to new cultures or for inoculating animals.

Thirty-two mongrel rabbits less than one day old were injected subcutaneously in the nuchal area with 1 ml. each of undiluted tissue-culture-grown virus of five different sub-lines[6]. 13–64 days later, 19 of the rabbits developed subcutaneous nodules—an incidence of 59 per cent. Most of the nodules were discrete, small and hard; some were large and filled with reddish or amber-coloured fluid. From the largest of such nodules 11 ml. of fluid was removed (Fig. 1).

Fig. 1. Multiple subcutaneous nodules induced in a rabbit 56 days of age by injection with *SE* polyoma virus when new-born

A nodule from a rabbit 56 days of age was minced and added to mouse embryo cell cultures and these cultures were maintained and fluid passed to new cell cultures, as has been described[1–4]. New-born hamsters, inoculated with 0·2 ml. each of fluid from second tissue-culture passage of this material, developed neoplasms in the heart and liver when 18 days old. Third tissue-culture passage of fluid from the *minced rabbit nodule showed cytopathic changes*[7] and fourth tissue-culture passage fluid was used for inoculating a litter of new-born rabbits. 1 ml. of tissue-culture fluid was injected into each rabbit. One rabbit developed subcutaneous nodules and died *at 13 days of age; another died on the fourteenth* day and no nodules could be found. Multiple subcutaneous nodules developed in each of the six remaining rabbits at 25 days of age. The results of the inoculation of rabbits with tissue-culture-grown *SE* polyoma virus *are summarized in Table 1. With the exception of* the last litter of rabbits that were injected with virus 63 days before, the nodules disappeared when the rabbits were 93–134 days old.

It may be noted that no tumours developed when *the animals were inoculated with one virus line*

Table 1. Induction of Subcutaneous Nodules in Rabbits Inoculated Subcutaneously when < 1 day of age with *SE* Polyoma Virus propagated in Mouse Embryo Cell Cultures

Virus line	Litter No.	No. of rabbits			
		Injected	Dead and *no nodules*	With *nodules*	Living and *no nodules*
3919	1	5	2	2	1
581	2	7	1	0	6
695	3	7	1	6*	0
877	4	3	0	3	0
877	5	2	1	1	0
R1517	6	8	1	7	0
Total		32		19 (59%)	

* Tissue from a subcutaneous nodule from one rabbit was used to initiate virus line *R1517*.

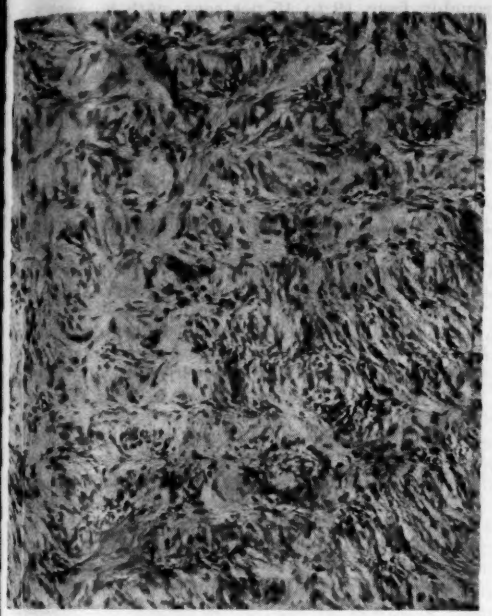

Fig. 2. A cellular area of a subcutaneous nodule. Interdigitating bundles of proliferating fibroblasts may be noted (hæmatoxylin and eosin). (× 135)

preparation. *In vitro* tests[7,8] had not been developed at the time these animals were injected, so it is unknown whether the tissue-culture fluid had a low virus content or whether the rabbits were resistant to the virus.

Nodules were excised from the living rabbits, fixed in Tellyesnicsky's formalin–acetic acid alcohol fluid[9], embedded, sectioned and stained with hæmatoxylin and eosin.

Histologically, the subcutaneous nodules were well circumscribed but not encapsulated (Fig. 2). There were interdigitating bundles of proliferating fibroblasts with plump nuclei seen against a background of pink collagenous tissue. The nodules were more cellular at the periphery and became relatively acellular toward the centre, when a tendency to form collagen was seen with an increase in hæmatoxylin-staining properties of the cells. In areas where cellular detail was sufficient the cells were fusiform with elongated nuclei and fibrillated cytoplasm. Some of the nodules were surrounded by a band of lymphocytes and neutrophils.

These nodules resembled certain fibrous growths in humans. They have been described and characterized by Stout[10] and are generally called fibromatoses. The fibrous growths are of limited growth potential and often regress as did the nodules in the rabbits.

The development of benign rather than malignant growths may be a reflexion of species differences in response of the host to the *SE* polyoma virus. The malignant growths in the different species of animals thus far studied vary. In the mouse, pleomorphic parotid gland tumours are most frequently seen but a variety of other neoplasms are also present. As many as eight histologically different tumours have been induced in one mouse. Multiple sarcomas and angiomatous lesions develop most often in the heart, liver and kidneys of the hamster, and sarcomas or angiomatous lesions occur in the kidneys or subcutaneous tissue of the rat.

(Since these experiments were completed, humoral antibodies for the *SE* polyoma virus have been demonstrated in rabbits after the nodules had regressed. Mice and hamsters bearing virus-induced tumours also develop humoral antibodies[11,12].)

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Freeze-drying of *Harposporium anguillulae* Lohde in its Nematode Host

RECENT attempts to use predacious fungi for the biological control of nematodes have shown the desirability of maintaining adequate supplies of infective material for laboratory and field studies. Many of these fungi can be grown in pure culture on synthetic media, but some grow with difficulty and others only in their hosts.

The freeze-drying of masses of fungus mycelium and spores might be a useful method of maintaining stocks of these obligate parasites. This was attempted using the endozoic fungus *Harposporium anguillulae* Lohde, which was recovered from the sandy soil of a Florida citrus grove infested with the burrowing nematode *Radopholus similis* (Cobb) Thorne. At this time, Aschner's[1] work on the isolation of this fungus in pure culture was not known, and the fungus was carried in living nematodes of the genera *Rhabditis* and *Panagrellus* growing on corn-meal agar plates. Cultures were readily transferred to disease-free nematodes growing on other corn-meal agar plates or swimming in tubes of sterile distilled water. Thousands of infected nematodes were reared in this fashion. The signs of infection appeared after 3–5 weeks at 22° C. Both types of cultures were freeze-dried.

The apparatus consisted of a 'Cenco Hyvac' pump, a 2-l. Dewar flask charged with a mixture of ethylene glycol and dry ice, a 2-l., three-necked flask for freezing the water vapour, and two 500-ml. drying flasks. All fittings were 'Pyrex' brand standard taper glass. The drying was carried out at about −28° C. and at a vacuum of less than 0·5 mm. of

mercury. The agar and fungus-infected nematodes were removed from the Petri dishes, placed in a Waring blendor, some sterile distilled water added and the mass homogenized for 1 min. The viscous mass was diluted with sterile distilled water to make up 100 ml. and 50 ml. were frozen into a thin film on the inner wall of each of the drying flasks, which were immediately evacuated. Drying took 8–10 hr. The resultant fluffy powder was dispensed into a glass jar which was sealed and kept at 22° C. Microscopic examination of the powder revealed large numbers of dead but intact nematodes, and the presence of mycelium and spores of *Harposporium* as well as other fungi.

At weekly intervals 10 mgm. lots of the powder were placed on corn-meal agar plates containing disease-free nematodes. After 3–5 weeks nematodes infected with *Harposporium* were observed, indicating that the viability and virulence of the frozen, dried fungus was not materially reduced. The disease developed in the usual manner and no morphological changes appeared in the fungus after freeze-drying. To date, the dried *Harposporium* powder has retained its activity and virulence for periods ranging up to 4 months from the date of drying.

In view of these results, attempts will be made to freeze-dry other predacious fungi, including those which can be readily grown in pure culture.

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GEOLOGY and PALÆONTOLOGY

How old is the Cambrian System?

In a recent contribution in *Nature*, Mayne, Lambert and York[1] have reported the results of age determinations on some British igneous rocks studied in the University of Oxford, and have concluded that the geological time-scale established in the works of Holmes (and of Marble and Belousov) is seriously in error. They claim that the age of 450 million years commonly assigned to Upper Cambrian strata is much too young, and that the base of the Cambrian System should be dated not at 500–520 m.y., but at about 750 m.y. This proposed drastic revision of the most significant date-line in geochronology conflicts somewhat with a large body of recent information to which, apparently, the authors have not had access.

The dating of the Cambrian system has hitherto been based largely upon determinations of the age of Swedish kolm, a mode of calibration which (as the Oxford authors correctly conclude) is very much open to criticism. Kolm is a uranium-rich hydrocarbon occurring within the trilobite sub-zones *Peltura minor* and *Peltura scarabaeoides* in the Upper Cambrian alum shales of Sweden, particularly in Närke and in the Billingen-Falbygden district of Västergötland. It forms lenses, sometimes coalescing into continuous seams, averaging 4 cm. but exceptionally reaching 20 cm. in thickness; and some twenty unpublished analyses of representative samples made for me when I carried out an economic survey of the Västergötland field in 1945 show an ash content roughly from 19 to 45 per cent, with between 2·91 and 0·51 per cent U_3O_8 in the ash. The oil-shale country-rock carries 0·02–0·04 per cent U_3O_8. The apparent age of the kolm, from determinations by Nier and by Cobb and Kulp[2], is: lead-206/uranium-238, 355–455 m.y.; lead-207/uranium-235, 420–480 m.y.; lead-207/lead-206, 650–945 m.y. This discordant pattern of these ages has been attributed by all previous workers to loss of radon and perhaps some loss of lead, notwithstanding an inability to demonstrate a high loss of radon at ordinary temperatures and the manifest incompatibility between hypotheses demanding loss of radon through notional thermal alteration and the presence in the alum shales of a commercial content (4–7 per cent) of oil.

The usefulness of kolm as a geochronological date-line rests wholly upon the hitherto undebated assumption that it acquired its uranium content when the associated trilobites were alive. But there is no evidence to support this premise and much to refute it. Many recent studies have shown that sedimentary hydrocarbons continue to adsorb uranium and other metals from percolating ground-waters long after they were deposited: as an extreme example, a Palæozoic coal may become enriched in uranium from a Mesozoic or Cainozoic radioactive deposit nearby. While, therefore, it seems likely that the kolm originated as a penecontemporaneous segregation of sapropelic gel during the diagenesis of the bituminous sediments, the probability is that for long after lithification it continued to adsorb uranium and perhaps a little lead. For the source of these metals, epigenetic to the kolm, one has to look no further than the surrounding uraniferous oil-shales, in which the metals are syngenetic. As these shales contain old radiogenic lead, the isotopic composition of lead within the kolm will not necessarily be related in any equivalent manner to the uranium there, though because of the extreme simplicity of the regional tectonics there will be but little local variation in the lead – uranium ratios. This interpretation explains the many chemical differences between the kolm and the shale (for example, the much higher sulphur content in the latter, calculated ash-free) and for the first time rationalizes the anomalous age determinations. The most that can be deduced from these figures is that the Upper Cambrian is younger than 650 m.y., the age given by the lowest recorded lead-207/lead-206 ratio.

Fortunately, the claim that "it would be particularly desirable to have unambiguous dates from the Ordovician and Cambrian"[1] has already been answered by Russian investigators[3–5]. For the earlier system a lower limit is set by the age of granite pebbles occurring in a Cambrian basement conglomerate in the Patomskoe uplands of Northern Irkutsk, where there is but a slight hiatus between Upper Proterozoic and Lower Cambrian strata. A granite pebble from this conglomerate gives a potassium/argon age of 464 m.y. determined on the rock, and 566 m.y. determined on mica from the rock. (Another pebble gives a value of 626 m.y., with 763 m.y. on the mica.) An upper limit is set by the Mainsk and Tannuol'sk granites of Tuva, which are intruded into Middle–Upper Cambrian strata and which shed pebbles into overlying Lower Ordovician conglomerates. The Tannu Ola granite is dated by Ivanova and Polevaya, in two potassium/argon determinations on the rock, at 443–448 m.y. Confirmatory determinations are to be found in an argon dating of basalt lava interstratified with reputedly Lower Cambrian (un-

fossiliferous) sediments in the Volynian series of Belorussia, with an age of 480 m.y., and in a comparable value, 490 m.y., arrived at for an extrusive porphyry interbedded with Lower Cambrian trilobite-bearing strata in Tuva. Even if these latter figures were increased by 20 per cent to bring 'rock-ages' (possibly low through escape of argon from feldspars) into line with 'mica-ages', the Lower Cambrian would not be more than 600 m.y. old.

Additional evidence of quite a novel kind, based on the calcium-40/potassium-40 ratio in sylvite, has just become available from the Radium Institute of Leningrad[6] in a paper which reports the age of a fossiliferous Lower Cambrian potash salt deposit in the Irkutsk region of 620 ± 20 m.y.

A greater age for the Cambrian system is also ruled out by the history of mineralization in Katanga, Belgian Congo[7,8]. Here the uraninite of Shinkolobwe, Kalongwe and Luishya has an age of 600–620 m.y., this being one of the firmest dates in the geological record; and this uranium mineralization is now known to have accompanied the last stages of folding in the Kundelungun geosyncline, at a period which cannot have greatly post-dated the youngest Kundelungun sediments[9,10]. These strata have locally a lithological character potentially very favourable to the preservation of fossils; but a full examination in the course of mining operations has demonstrated that they are devoid of vestiges of life other than stromatolites, micro-algæ and sponge spicules. In other words, at round about 650 m.y. ago a Cambrian fauna had not yet developed.

Recently, Polevaya[3] has published argon datings on twenty-nine post-Proterozoic lavas collected from known geological horizons throughout the stratigraphical column. All but one of her values, without any correction for argon leakage, fit quite well into the Holmes-Marble scale. That loss of argon must have taken place is nevertheless evident from Gerling's extensive studies on the White Sea pegmatites[4], where the average argon leakage from feldspar is 23 per cent, argon datings on micas agreeing excellently with well-established uranium ages. Presumably, therefore, an empirical correction not exceeding 20 per cent must be made in the argon dating of rocks such as liparites, felsites and porphyries when the determination is made on the whole rock and not on separated mica. Such a correction will result in an extension of the Holmes scale going nearly half-way towards the proposals of the Oxford group. On this revised chronology, the base of the Cambrian is dated at about 600 m.y.

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Prof. C. F. Davidson has presented no new evidence free from unambiguous interpretation which would refute our proposed extension of the Holmes *B* time-scale; or indeed on which an alternative scale could be based. The examples which he cites form only a part of a large number of such data which we have considered. We have rejected them because either the stratigraphy of the samples or their measured age is not free from unwarranted assumptions. We have used only samples which are above criticism on these points. We would, however, like to correct Prof. Davidson's remark that we "claim that the base of the Cambrian System should be . . . at about 750 m.y.". In fact, we have avoided using the rather meaningless term 'base of the Cambrian', and we have but estimated, by extrapolation from our oldest measured date at around 500 m.y., that the upper Cambrian "should be closer to 650 m.y.". Prof. Davidson's recapitulation of a possible geochemical history of the kolm emphasizes our conclusion that this material provides a poor calibration point. The pattern of discordancy[1] found for lead ages of the kolm material would not justify his argument that the kolm is younger than 650 m.y. Nevertheless, such an age is not incompatible with an extrapolation of our scale. Considering that the precision of measurement is not better than 5 per cent, this extrapolation could give an age for the top of the Cambrian between 600 and 650 m.y., and clearly this age also depends greatly on the (unknown) length of the Ordovician.

It has been known for a long time that loss of radiogenic argon can occur to a variable extent in some minerals which show no apparent alteration, notably potassium felspar. Thus Prof. Davidson's interpretation of the Russian argon/potassium age values is not justified. This variable loss is often found to be greater than the 23 per cent measured by Gerling for pegmatitic felspar from a particular locality. Its extent is unpredictable *a priori* in any particular sample, although many measurements in the range 300–600 m.y. show a loss greater than 30 per cent. (It is because of this uncertainty that we attach little importance to our interpretation of the age of the Mynydd Mawr microgranite, and the Dubuque felspar.) It is therefore meaningless to use an average percentage loss in order to assess the true age with sufficient precision from whole rock analysis. The whole-rock age-value of lavas and similar very fine-grained rocks may be even more seriously affected on account of the extremely fine grain of the potassium minerals in it. Whole-rock analysis is not yet sufficiently precise for defining a time-scale; and there is certainly no foundation for presuming that "an empirical correction not exceeding 20 per cent must be made in the argon dating of rocks such as liparites, felsites and porphyries, when the determination is made on the whole rock and not on separated mica". In fact, the empirical correction would be particular to each sample, and largely unknown—especially for lavas. Thus the only Russian measurements which are relevant are those on the mica separated from granite pebbles found in Lower Cambrian rocks. Two values are given, 566 m.y. and 763 m.y., and there seems to be no reason to prefer the younger of these as Davidson has done, or indeed, with such disagreement, either of them.

The calcium–potassium method of dating was first used by Inghram *et al.*[2]. The results of its application have shown poor agreement with best-age values, and the analytical errors may be high[2]. Sylvite is an

unsuitable mineral to use for dating geological events, since it is subject to recrystallization. We have no knowledge of the geological or analytical details of the Leningrad sample, so it is difficult for us to decide if it fulfils the stringent requirements of a calibration sample. The problem of dating the Ordovician and Cambrian remains.

A close examination of the geology of the Shinkolobwe uranium deposit shows that it is far from being "one of the most certain points in the geologic time scale" (Prof. J. L. Kulp, in Robert, ref. 4, p. 17). Thus, although the age of 630 ± 35 m.y. (as quoted by Robert) is generally agreed to be unusually good, the Shinkolobwe deposit is of no use in defining a time-scale. The precise facts are that the uranium minerals are present in veins of mesothermal type occurring within folded dolomites of the Système Schisto-dolomitique of Katanga. These dolomites and other similarly folded dolomites overlying them in nearby areas contain *Collenia* and *Stromatolithes*, fossils known to exist from the early pre-Cambrian to the Cambro-Ordovician inclusive. The stratigraphic definition of the uranium deposits is therefore of the poorest. The absence of ordinary marine lower-palæozoic faunas is of no weight in this argument, as they are generally unknown from South and Central Africa. We have discussed these remarks on the African samples with Prof. J. L. Kulp, and we learn that his original statement did not refer to the stratigraphy, but to the measured age.

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Synthetic Carbonatite Magma

Judging from the literature during the past decade, there is a growing interest in problems related to the genesis of carbonatites and associated alkaline igneous rocks. The interest has undoubtedly been fostered by the discovery of large reserves of rare earths in these rocks. Many field geologists believe that carbonatites were emplaced as liquid magmas; but hitherto there has been no conclusive experimental evidence to support the existence of carbonatite liquids. In fact, from the available experimental evidence it seemed unlikely that such liquids could exist at the low temperatures indicated by field studies. We have recently obtained experimental evidence that simplified carbonatite magmas can exist at moderate temperatures through a wide range of pressures.

Results[1] from a study of the join calcite–water in the ternary system $CaO–CO_2–H_2O$ show that calcite begins to melt at a temperature of 740° C. at 1,000 bars pressure of water vapour. Only a trace of liquid was developed at this temperature, but the amount increased with increasing water content and with increasing temperature. This evidence implied, but did not prove, the existence of carbonatite magmas.

Subsequent studies on the system $CaO–CO_2–H_2O$ have shown that the minimum liquidus temperature at 1,000 bars pressure is 675° C. ± 5° C. At this temperature and pressure, a liquid with the composition calcium oxide 64, carbon dioxide 18, water 18 (weight per cent) is in equilibrium with calcite, portlandite and vapour (almost pure water). At 680° C. and the same pressure, a liquid develops on the calcium oxide side of the $Ca(OH)_2–CaCO_3$ join; this is in equilibrium with calcite, portlandite and calcium oxide and has a composition calcium oxide 68, carbon dioxide 19, water 13 (weight per cent). At 685° C. the two liquid fields coalesce and at still higher temperatures the range of composition of the liquid field increases. The minimum liquidus temperature in the system has been determined for a range of pressures. At 500 bars the temperature is 680° C., and at 4,000 bars it is lowered to 640° C. At pressures lower than 50 bars, the minimum liquidus temperature decreases, and at 27 bars pressure the appropriate composition is completely liquid at 665° C. The high melting temperature of calcite is therefore lowered markedly by the addition of calcium oxide and water under pressure. The low-temperature liquid may be regarded as a simplified carbonatite magma. Although calcite is generally the dominant mineral in carbonatites, dolomite is frequently an important constituent, while apatite and mica are constant accessories. Experiments are under way to find the effect of additional components (such as magnesium oxide, phosphorus pentoxide, silicon dioxide and alkalis) on the minimum liquidus temperature in the ternary system. Solubility determinations are also being made to see how the solubility of calcite varies with increasing content of carbon dioxide in the aqueous vapour phase. Many geologists believe that a high-temperature vapour, consisting of water and carbon dioxide, is able to dissolve large amounts of calcium oxide, magnesium oxide, ferrous oxide, etc.

Detailed results of these studies will be published in due course, but we take this opportunity of presenting these facts now because they will be of interest to geologists working on carbonatites.

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Manganese in Modern and Fossil Gastropod Shells

Very little work has been done on manganese concentrations in shell material and particularly in gastropod shells, although Doring in Vinogradov's book[1] reported several analyses and found from 0·1 to 0·0001 per cent manganese by weight in gastropod shells. Krinsley and Bieri[2] have determined manganese in the shells of modern and fossil pteropods.

This trace element was examined in modern and fossil shells to determine whether burial and subsequent diagenesis might have altered the original material.

Eighty modern and fossil shells of *Olivella biplicata* (Sowerby), 89 of *Tegula funebralis* (A. Adams) and

Table 1

Locality	*Olivella* Mn (p.p.m.) $\bar{x}$	*Olivella* Ar. (per cent) $\bar{x}$	*Olivella* No. of specimens	*Tegula* Mn (p.p.m.) $\bar{x}$	*Tegula* Ar. (per cent) $\bar{x}$	*Tegula* No. of specimens	*Fissurella* Mn (p.p.m.) $\bar{x}$	*Fissurella* Ar. (per cent) $\bar{x}$	*Fissurella* No. of specimens
MODERN ANIMALS									
A La Jolla, California 32° 52′ N., 117° 16′ W.	4	100	10	5	54	10	7	66	10
B La Jolla, California 32° 52′ N., 117° 16′ W.	< 4	100	10	6	64	10	< 4	60	10
C Palos Verdes, California 33° 47′ N., 118° 25′ W.	5	100	10	4	92	10	6	61	10
D Palos Verdes, California 33° 47′ N., 118° 25′ W.				6	67	10			
E Pismo Beach, California 35° 10′ N., 120° 40′ W.	< 4	100	9	4	75	9	< 4	53	10
F Neah Bay, Washington 48° 40′ N., 124° 40′ W.	< 4	100	10	5	65	10			
FOSSILS									
X Upper Pleistocene. Ocean Beach, California 32° 42′ N., 117° 16′ W.	8	100	10	13	70	10	5	57	9
Y Middle Pleistocene Pacific Beach, California 32° 48′ N., 117° 16′ W.	4	100	10	17	87	10			
Z Middle Pleistocene San Pedro, California 33° 45′ N., 118° 17′ W.	11	100	10	17	81	10			

Localities *Y* and *Z* represent equivalent ages.

49 of *Fissurella volcano* Reeve were analysed for manganese with a 21-ft. grating spectrograph[3]. Aragonite percentages were determined with a North American Phillips X-ray diffraction unit, using the method reported by Chave[4] with modification. (Note that each locality listed in Table 1 represents the mean of approximately ten specimens analysed in duplicate.) The specimens were carefully hand-cleaned to eliminate any material on external and internal shell surfaces. The error involved in the spectrographic analyses was ± 20 per cent of the amount present.

Since manganese, because of its size, will theoretically fit more readily into the calcite than the aragonite structure, one would expect to find more manganese in calcitic shells than aragonitic ones. However, the amount of manganese in the shell material analysed is small, and the results are inconclusive (Table 1) with respect to modern specimens.

Post-depositional changes have increased the amount of manganese in some of the fossil shells (Table 1). *Tegula* and *Olivella* fossil shells have more manganese than modern shells with the exception of *Olivella* at locality *Y*, which has the same amount as modern specimens. *Fissurella* modern and fossil shells contain the same concentrations of manganese. One might at first suspect that the larger manganese concentrations in some of the fossils were due to surface contamination from the sediment matrix, even though the specimens were carefully cleaned. However, this is shown to be unlikely by the 19 analyses of fossil *Fissurella* at locality *X* and *Olivella* at locality *Y*, which do not differ from the modern shells.

No recrystallization of shell material has occurred in *Olivella* as indicated by lack of change in calcite-aragonite ratios in the fossils. Probably little or no recrystallization has occurred in *Tegula*; the aragonite percentages in fossil *Tegula* are higher than those in modern forms. Recrystallization always lowers the aragonite content.

Two groups of *Tegula* specimens were selected at Palos Verdes, California (Table 1). Group *D* was collected alive on rocks at the edge of the beach and killed, while group *C* was collected from shell heaps on the beach. All other *Tegula* specimens were collected alive. The age of group *C* is impossible to determine; but the shells have undoubtedly been subjected to alternate wetting and drying after death or may even have been under water for some time. In any event, no increase in manganese has occurred in group *C*, indicating that the processes which have added manganese to the shells probably occur largely after burial.

If the mean manganese content at a given fossil locality in a particular species is higher than in modern specimens, then the manganese variation in that population is found to be correspondingly high. Manganese would be expected to accumulate at different rates in individual fossils and thereby increase variation in the fossil populations. This increased variation, which is not characteristic of any of the modern specimens, is another indication that addition of manganese has occurred after burial. If no alteration of the shell material at a particular fossil locality has occurred, fossil variation will approximate modern variation.

The increase in manganese in some of the fossils is due partially to diffusion from the surrounding sediments into the shell material (assuming that the fossils originally had approximately the same composition as the modern animals). The size of the shell crystals, the differing construction of shell material in the various species examined[5], chance contact with other shells of higher manganese content and, more important, diagenetic conditions at a particular locality, probably determine whether increase of manganese in fossil shells has occurred. It is impossible at present to separate these factors; but diffusion experiments and a more thorough knowledge of the construction of shell material should help solve the problem.

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STATISTICS

Matching and Prediction in the Social Sciences

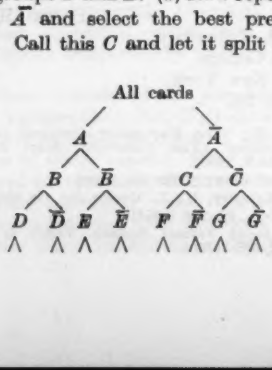
Matching processes are constantly in use in the social sciences. Often their use is explicit, as in studies of the relative effects of different experiences or procedures. In other cases they are implicit, as in the use of specific controls for the selection of consumer panels or in quota surveys. They are also implicit in many extrapolation processes. Even so, the variables used for matching processes are in most cases of non-empirical origin, and are selected on the basis of either custom or hunch. The result may well be that the matching is inadequate, sometimes completely so.

Empirical procedures can, of course, be used. The principle of the empirical method is that, for a variable to be relevant in matching, it must be correlated to some appreciable degree with whatever it is that is being studied (for example, a specific attitude, buying behaviour). If all the proposed matching variables are arranged in a correlation matrix, multiple correlation methods[1] can be used to select from them that combination of variables which gives the highest multiple correlation with whatever is being studied (that is, the criterion). These variables are then used as the basis for matching, and this usually proceeds through a form of prediction, perhaps involving the use of a regression equation.

This sort of work is, however, most arduous. Matching on the empirical principle requires that each fresh criterion must have its own set of matching variables. Also, the development of a correlation matrix is specially inadequate where many of the available variables involve a 'yes' or 'no' response.

Several years ago I developed a technique of the latter kind and have used it in various inquiries[2,3]. But a much simpler and more adequate technique can be used, and I have applied this in more recent studies[4].

The method involves matching on the principle of simple classification. Suppose the matching is being done to allow the study of the effect of different stimuli on criterion X. The following steps are involved. (*a*) Numerous proposed matching variables are included in the testing phase. (*b*) Each of them is then analysed against score on criterion X, and that one which has the greatest association with, or power to predict, the criterion score is selected as the first-stage predictor (or matching variable). This variable will then serve to split the record cards of the informants into at least two groups, A and $\bar{A}$. (*c*) Next, this process is repeated with all the cards in pack A, and the variable with the highest predictive power is selected as the second-stage predictor within that pack. Call this one B, and let it split the A pack into groups B and $\bar{B}$. (*d*) Now repeat the process with pack $\bar{A}$ and select the best predictor within that pack. Call this C and let it split $\bar{A}$ into C and $\bar{C}$.



The vital point here is that the second-stage predictor in pack A is not necessarily the same as the second-stage predictor in pack $\bar{A}$. In other words, what matters in one group may well differ from what matters in another. Multiple correlation procedures do not allow for this. (*e*) The splitting process is continued, so far as it can be taken, on the pattern shown above. The final set of categories or sub-groups defines the matching composite.

There is no need to employ only two-way splits of card packs. Three or more splits can be used at any stage.

The device for selecting any one predictor in the composite is a simplified version of the chi square calculation. The cards are analysed on a four-cell system: 'high' versus 'low' scores on the criterion test and 'yes' versus 'no' on the item being tested as a possible matching variable. The matching power of this trial item is given in the form of a direct count of the number of cases in the four cells which deviate from what might be expected on a null hypothesis (that is, a hypothesis of no association or predictive power at all). Matching power so derived is more accurate than when gauged from most correlation coefficients. It is on the basis of this selection procedure that the final matching composite is built up as described above.

The use of the selected composite of matching variables to achieve matching is also very straightforward. Suppose that in the study of criterion X (for example, buying behaviour), the record cards for sample I are to be matched to those for sample II. (*a*) Split each sample into sub-groups on the above pattern. Suppose this yields 40 sub-groups (for each sample). (*b*) Now equate the number of cards in each sub-group (in the sample I pack) to its equivalent sub-group in the sample II pack. This can be done on random principles, but the equating process must not involve throwing out more than a few record cards. Discarding of cards can be all but avoided if the device is used of multiplying all the pack II sub-groups by a constant sufficient to raise their numbers well above the general level of the numbers in pack I. This constant may be 2 or 3 or 4 depending on the relative sizes of the two samples. (*c*) Alternatively, the average criterion score for each sub-group in pack I can be weighted (separately) by the number of cards in the equivalent sub-group in pack II. In this way, there need be no loss of cards at all, though slight statistical problems may arise.

I have been using the 'classification system' of matching since 1957. There are points at which it is similar to the technique described in the recent communication by Williams and Lance[5].

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FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, March 16

ROYAL INSTITUTION, LIBRARY CIRCLE (at 21 Albemarle Street, London, W.1), at 5.30 p.m.—Four short talks on "Books from the R.I. Library".

SOCIETY OF CHEMICAL INDUSTRY, PESTICIDES GROUP (at 14 Belgrave Square, London, S.W.1), at 5.30 p.m.—Mr. J. E. H. Grose: "Problems in Stomoxys Research in East Africa".

INSTITUTION OF ELECTRICAL ENGINEERS, LONDON GRADUATE AND STUDENT SECTION (at Savoy Place, London, W.C.2), at 6 p.m.—Mr. G. O. McLean: "Something for Nothing? Heat Pump Achievements".

NORTHAMPTON COLLEGE OF ADVANCED TECHNOLOGY (at St. John Street, London, E.C.1), at 6 p.m.—Dr. Dimitri Riabouchinsky (L'Académie des Sciences de l'Institut de France): "The Hydraulic Analogy and Air Resistance".

INSTITUTE OF METAL FINISHING (at the Northampton College of Advanced Technology, St. John Street, London, E.C.1), at 6.15 p.m.—Prof. Ernst Raub: "Hydrogen Content of Electro-Deposits".

Tuesday, March 17

INSTITUTION OF CHEMICAL ENGINEERS (at Church House, Westminster, London, S.W.1), at 9.30 a.m.—Spring Meeting.

INSTITUTION OF ELECTRICAL ENGINEERS, MEASUREMENT AND CONTROL SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. G. Phillips: Informal lecture on "Electrical Uses of Atomic Spin".

PLASTICS INSTITUTE, LONDON AND DISTRICT SECTION (at the Wellcome Building, 183–193 Euston Road, London, N.W.1), at 6.30 p.m.—Mr. D. S. Mahon: "Plastics—Why should I Worry?" (Chairman's Lecture).

Tuesday, March 17—Thursday, March 19

OIL AND COLOUR CHEMISTS' ASSOCIATION (at the Royal Horticultural Society's New Hall, Greycoat and Elverton Streets, London, S.W.1)—Eleventh Technical Exhibition.*

Tuesday, March 17—Saturday, March 21

EIGHTH ELECTRICAL ENGINEERS (A.S.E.E.) EXHIBITION (at Earls Court, London).

Wednesday, March 18

ROYAL SOCIETY OF ARTS (at John Adam Street, Adelphi, London, W.C.2), at 2.30 p.m.—Dr. B. A. Southgate: "A Study of the Pollution of the Thames Estuary".

PHYSICAL SOCIETY, COLOUR GROUP (at the Institute of Ophthalmology, Judd Street, London, W.C.1), at 3 p.m.—Mr. A. W. S. Tarrant: "How Reproducible are Standard Illuminants?". 4.45 p.m.—Discussion on "Illuminants B and C" introduced by Mr. J. Guild and Mr. F. Warburton.

GEOLOGICAL SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Prof. B. C. King: "Problems of Pre-Cambrian Correlation in Western and Central Uganda".

ROYAL METEOROLOGICAL SOCIETY (at 49 Cromwell Road, London, S.W.7), at 5 p.m.—Mr. H. H. Lamb: "The Southern Westerlies—a Preliminary Survey; Main Characteristics and Apparent Associations"; Mr. W. T. Roach and Mr. R. M. Goody: "Absorption and Emission in the Atmospheric Window from 770 to 1,250 cm.$^{-1}$".

ROYAL STATISTICAL SOCIETY (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.15 p.m.—Mr. W. E. Thomson: "ERNIE—a Mathematical and Statistical Analysis".

EUGENICS SOCIETY (at the Royal Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Mr. R. W. Parnell: "Physique and Family Structure".*

INSTITUTION OF ELECTRICAL ENGINEERS, RADIO AND TELECOMMUNICATION SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. C. W. Oatley: "New Amplifying Techniques".

ROYAL INSTITUTE OF CHEMISTRY; THE CLASSICAL ASSOCIATION; and the HALDANE SOCIETY (at the William Beveridge Hall, Senate House, University of London, W.C.1), at 5.30 p.m.—Debate on the motion "That the Education of our Future Rulers should be Primarily in the Sciences rather than in the Humanities". Chairman: Prof. Sir Cyril Hinshelwood, F.R.S. Proposer, Sir Alexander Fleck, K.B.E., F.R.S. Opposer: Prof. B. Farrington. Seconder for the Motion: Prof. A. R. Ubbelhode, F.R.S. Seconder against the Motion: Prof. W. Beare.

UNIVERSITY COLLEGE, DEPARTMENT OF PHARMACOLOGY (in the Physiology Theatre, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. Valy Menkin (Temple University, Philadelphia): "Biochemical Mechanisms Involved in Inflammation".*

BRITISH COMPUTER SOCIETY (at the Northampton College of Advanced Technology, St. John Street, London, E.C.1), at 6.15 p.m.—Mr. C. E. G. Bailey: "An Approach to Learning and Teaching Machines".

SOCIETY OF CHEMICAL INDUSTRY, CORROSION GROUP (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Mr. A. Keynes: "Economic Aspects of Corrosion".

Thursday, March 19

PHYSICAL SOCIETY, OPTICAL GROUP (in the Physics Department, Imperial College, London, S.W.7), at 2.30 p.m.—18th Annual General Meeting.

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.15 p.m.—Meeting for Election of Fellows. 4.30 p.m.—Mr. D. Brennan and Mr. P. C. Fletcher: "The Atomization of Hydrogen on Tungsten"; Mr. G. A. Gilbert: "Sedimentation and Electrophoresis of Interacting Substances. 1: Idealized Boundary Shape for a Single Substance Aggregating Reversibly".

INSTITUTION OF MINING AND METALLURGY (at the Geological Society of London, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Mr. F. A. Williams: "Recovery of Semiheavy Minerals in Jigs"; Mr. D. C. Shelton: "Santa Barbara Mill, Chihuahua, Mexico".

LINNEAN SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Dr. Kathleen I. M. Chesters: "Ecological Conditions in the Early Tertiary of Great Britain"; Prof. Tom Harris F.R.S.: "The Possibilities of Palæo-ecology in the Jurassic"; Dr. William S. Lacey: "Some Aspects of Palæo-ecology in the Karroo of Rhodesia and Nyasaland".

LONDON MATHEMATICAL SOCIETY (at the Royal Astronomical Society, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Prof. B. Huppert: "Composition-series of Finite Groups".

ROYAL AERONAUTICAL SOCIETY (at the Institution of Civil Engineers, Great George Street, London, S.W.1), at 6 p.m.—Mr. E. C. Cornford: "Long Range Missiles".

SOCIETY OF CHEMICAL INDUSTRY, ROAD AND BUILDING MATERIALS GROUP (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Mr. D. A. Dowdeswell: "Slag for Roadmaking".

BRITISH INSTITUTION OF RADIO ENGINEERS, MEDICAL ELECTRONICS GROUP (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6.30 p.m.—Dr. H. Wolff: "Instrumentation in Field Physiology".

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE (at the Royal Army Medical College, Millbank, London, S.W.1), at 7.30 p.m.—Laboratory Meeting. Chairman: Sir John Boyd, O.B.E., F.R.S.

BRITISH INSTITUTE OF RADIOLOGY, incorporated with the ROENTGEN SOCIETY (at 32 Welbeck Street, London, W.1), at 8 p.m.—Mr. D. A. Wilson: "Some Health and Safety Problems".

Thursday, March 19—Friday, March 20

PHYSICAL SOCIETY (at Birkbeck College, Malet Street, London, W.C.1), at 9.30 a.m. daily—Symposium on "Fluctuation Phenomena and Stochastic Processes".

SOCIETY OF CHEMICAL INDUSTRY, LONDON SECTION (in the Beveridge Hall, Senate House, University of London, W.C.1), at 2.15 p.m. on Thursday and 9.30 a.m. on Friday—Symposium on "Costing in the Chemical Industry".

INSTITUTION OF ELECTRICAL ENGINEERS, RADIO AND TELECOMMUNICATION SECTION (at Savoy Place, London, W.C.2)—Convention on "Stereophonic Sound Recording, Reproduction and Broadcasting".

NATIONAL ASSOCIATION FOR MENTAL HEALTH (at the Assembly Hall, Church House, Westminster, London, S.W.1), at 10 a.m. daily—Conference on "The Place of Work in the Treatment of Mental Disorder".

Friday, March 20

SOCIETY FOR WATER TREATMENT AND EXAMINATION (in the Library, Royal Society of Health, 90 Buckingham Palace Road, London, S.W.1), at 9.30 a.m.—Seventh Annual General Meeting.

BIOCHEMICAL SOCIETY (in the Department of Biochemistry, The University, South Parks Road, Oxford), at 11 a.m.—381st Meeting.

ROYAL ASTRONOMICAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.15 p.m.—Discussion of geophysical papers received during the Session. Chairman: Dr. R. Stoneley, F.R.S. Speakers will include Dr. A. H. Cook, Mr. C. Jones and Dr. R. L. G. Gilbert.*

INSTITUTE OF NAVIGATION (at the Royal Geographical Society, 1 Kensington Gore, London, S.W.7), at 5.15 p.m.—Captain F. J. Wylie, R.N.: "The Impact of Radar on the Rules of the Road at Sea".

INSTITUTION OF ELECTRICAL ENGINEERS (joint meeting with the INSTITUTIONS OF CIVIL AND OF MECHANICAL ENGINEERS, at the Institution of Mechanical Engineers, 1 Birdcage Walk, London, S.W.1), at 6 p.m.—Sir Harold Plant: Fifth Graham Clark Lecture.

INSTITUTION OF ELECTRONICS (in the Assembly Hall of the University of London Institute of Education, Malet Street, London, W.C.1), at 7 p.m.—Mr. L. E. A. Bourn: "The Electronic Organ".

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 9 p.m.—Air Commodore W. K. Stewart: "Man as a Controller of Flight Vehicles".

Saturday, March 21

LINNEAN SOCIETY OF LONDON, PALÆOBOTANY GROUP (at Burlington House, Piccadilly, London, W.1), at 11 a.m.—Discussion on certain of the Proposals concerning the International Code of Botanical Nomenclature.

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

LECTURER IN BIOCHEMISTRY—The Registrar, The Manchester College of Science and Technology, Manchester 1 (March 28).

Chair of Forensic Medicine; and Chair of Bacteriology in the University of Ceylon—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Ceylon, March 31).

Assistant Lecturers (2) in Pure Mathematics; Assistant Lecturers or Lecturers (3) in Applied Mathematics; a Lecturer in Statistics; an Assistant Lecturer (with special interests in experimental morphology or physiological ecology) in Botany; Junior Research Fellows (2) (with special interests in organic or inorganic chemistry) in Chemistry; a Lecturer (medically qualified) in Medical Genetics; and a Lecturer in Biochemistry—The Registrar, The University, Sheffield (April 4).

Assistant Lecturers or Lecturers in Pure Mathematics (two appointments); Physics, Civil Engineering, Mechanical Engineering, and Chemical Engineering; and an Assistant Lecturer in Geology—The Registrar, University College, Singleton Park, Swansea (April 4).

Research Assistant in the Department of Botany, to assist with research on aspects of nitrogen metabolism being conducted by Dr. G. E. Fogg and Dr. L. Fowden—The Secretary, University College, Gower Street, London, W.C.1 (April 4).

Senior Lecturer in Physics—The Registrar, The University, Sheffield (April 4).

Imperial Chemical Industries Fellows (preferably under 29 years of age) at Durham or Newcastle, for research in Engineering, Chemistry, Physics and allied subjects, including the biological application of chemistry—The Registrar, University Office, 46 North Bailey, Durham (April 6).

Research Fellow (with a Ph.D. degree or equivalent research experience) in the Chemistry Department, for work on fundamental aspects of heterogeneous catalysis, in collaboration with Dr. G. C. Bond—The Professor of Chemistry, The University, Hull (April 6).

Research Fellow (with a Ph.D. degree or equivalent research experience) in the Chemistry Department, for work on the kinetics of gaseous oxidation reactions, in collaboration with Dr. R. R. Baldwin—The Professor of Chemistry, The University, Hull (April 6).

Chair of Philosophy—The Registrar, University Office, 46 North Bailey, Durham (April 9).

Research Fellow (with an interest in physical-organic chemistry, and some postgraduate experience in preparative chemistry) in the Department of Chemistry—The Registrar, Queen Mary College (University of London), Mile End Road, London, E.1 (April 10).

Lecturer in Mathematics—The Secretary, The University, Aberdeen (April 11).

Lecturer (with good academic qualifications) in Botany—The Clerk to the Governors, Chelsea College of Science and Technology, Manresa Road, London, S.W.3 (April 13).

Lecturer in Physiology—The Secretary, The Queen's University, Belfast (April 15).

Lecturer in the Department of Metallurgy, to teach and carry out research in Physical Metallurgy—The Registrar, The University, Liverpool (April 18).

Lecturer or Assistant Lecturer in Experimental or Theoretical Physics at the University College of the West Indies—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (April 18).

Assistant Lecturer (honours graduate) in Chemistry—The Secretary, Bedford College (University of London), Regent's Park, London, N.W.1 (April 20).

Reader or Senior Lecturer in Soil Science; a Senior Lecturer or Lecturer in Horticulture; and a Senior Lecturer or Lecturer in Farm Mechanization and Irrigation at the University of Khartoum—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (April 20).

Assistant Director (with a good degree or equivalent qualification in a biological science, experience of annual and perennial crops, and preferably a knowledge of foreign languages and experience in editing scientific publications) of the Bureau of Horticulture and Plantation Crops, East Malling Research Station, East Malling, Maidstone, Kent—The Secretary, Commonwealth Agricultural Bureaux, Farnham House, Farnham Royal, Bucks (June 14).

Assistant Master to teach Mathematics up to University Scholarship level—The Headmaster, Tonbridge School, Tonbridge, Kent.

Head of the Chemistry Department—The Headmaster, Gordonstoun School, Elgin.

Master (not over 30, with at least a second-class honours degree) to teach Physics up to Lower Sixth form standard—The Headmaster, King's College School, Wimbledon, S.W.19.

Scientific Officer or Senior Scientific Officer (with a good honours degree or equivalent with training preferably in both physiology and physics), for research in the energy metabolism of farm animals using direct calorimetry—The Secretary, Rowett Research Institute, Bucksburn, Aberdeenshire.

Seed Mycologist (with a degree in botany, and preferably some postgraduate training) on the staff of the Official Seed Testing Station for England and Wales—The Secretary, National Institute of Agricultural Botany, Huntingdon Road, Cambridge.

Senior Scientific/Scientific Officer (with a first- or second-class honours degree in physics or physical chemistry or equivalent qualifications), to carry out research concerned with the development and application of solid-state electronic optical devices—The Senior Recruitment Officer, Atomic Weapons Research Establishment, Aldermaston, Berkshire, quoting Ref. 2174/34.

Soil Chemist (with an honours degree in chemistry, or in natural science including chemistry, and at least two years postgraduate training or experience as a Soil Chemist) at the West African Institute for Oil Palm Research, Nigeria, for the study and analysis of soil types with a view to improving soil conditions—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.197/199/016.

Statistician (with a good honours degree and preferably experience or an interest in agricultural experimentation) in the Department of Biometrics—The Secretary, The Grassland Research Institute, Hurley, near Maidenhead, Berks.

Technician or Junior Technician (G.C.E. (A) standard), for biochemical and histological research—The Professor of Pathology, Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.2, marking envelope "Path. Technician".

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences. No. 687, Vol. 242 (1 January, 1959): Observations on the Solenacea with Reasons for Excluding the Family Glaucomyidae. By G. Owen. Pp. 59–97. 12*s*. No. 688, Vol. 242 (1 January, 1959): A Study of Variation and Relative Growth in the Blastoid *Orbitremites*. By K. A. Joysey. Pp. 99–125. 10*s*. (London: Royal Society, 1959.) [11

Observations Made at the Royal Observatory, Greenwich, in the year 1957 in Astronomy, Magnetism and Meteorology. Pp. 442. (London: H.M. Stationery Office, 1958.) 117*s*. 6*d*. net. [11

The Health of the School Child: Fifty years of the School Health Service. (Report of the Chief Medical Officer of the Ministry of Education for the years 1956 and 1957.) Pp. i+220+12 plates. (London: H.M. Stationery Office, 1958.) 10*s*. 6*d*. net. [191

Government of Northern Ireland: Ministry of Agriculture. Leaflet No. 110: Diseases and Pests of Tomatoes. Pp. 14. (Belfast: Ministry of Agriculture, 1958.) [191

Planning, Vol. 25, No. 430: Scientific and Engineering Manpower Survey. By Richard Fort, M.P. Pp. 1–128. (London: Political and Economic Planning, 1959.) 2*s*. 6*d*. [191

Northampton College of Advanced Technology. Report of the Governing Body for the year 1957–58. Pp. 18. (London: Northampton College of Advanced Technology, 1959.) [191

The Colombo Plan for Co-operative Economic Development in South and South-East Asia—Seventh Annual Report of the Consultative Committee, Seattle, Washington, November 1958. Pp. 192. (Cmnd. 610.) (London: H.M. Stationery Office, 1958.) 8*s*. net. [191

National Parks and Access to the Countryside Act. Ninth Report of the National Parks Commission for the year ending September 30, 1958. Pp. iv+79+8 plates. (London: H.M. Stationery Office, 1958.) 5*s*. 6*d*. net. [191

Other Countries

The Transvaal Ape-Man—Bearing Cave Deposits. By C. K. Brain. With an Appendix by R. F. Ewer. (Transvaal Museum Memoir No. 11.) Pp. viii+131. (Pretoria: Transvaal Museum, 1958.) [11

Rijkslandbouwhogeschool, Gent. Tiende International Symposium over Fytofarmacie en Fytiatrie, 6–7, Mei, 1958. (Overdruk uit Mededelingen van de Landbouwhogeschool en de Opzoekingsstations van de Staat te Gent, 1958, Deel XXIII, No. 3–4.) Pp. viii+561-1056. (Gent: Rijkslandbouwhogeschool, 1958.) [11

Institut Royal Meteorologique de Belgique. Publications Serie A, No. 7: Realisation du Centre de Physique du Globe a Dourbes. Par Prof. Edm. Lahaye. Pp. 104. (Bruxelles: Institut Royale Meteorologique de Belgique, 1958.) [11

Conseil International des Unions Scientifiques. Union Géodésique et Géophysique Internationale. Association de Séismologie et de Physique de l'Intérieur de la Terre. Comptes Rendus des Séances de la Onzième Conférence Réunie a Toronto du 3 au 14 Septembre 1957. (Comptes Rendus No. 12.) Pp. 448. (Strasbourg: Bureau Central International de Séismologie, 1958.) [191

Organisation for European Economic Co-operation. Third Report on the Agricultural Policies in Europe and North America. (Report prepared by the Ministerial Committee for Agriculture and Food.) Pp. 467. (Paris: Organisation for European Economic Co-operation; London: H.M. Stationery Office, 1958.) 1,400 francs; 24*s*. [191

Rockefeller Foundation. The President's Review from the Rockefeller Foundation Annual Report, 1957. Pp. viii+75+31 plates. (New York: Rockefeller Foundation, 1958.) [191

Caracteristicas de Alguns Oleos Essencias Brasileiros. By Waldemar Raoul. Pp. 24. (Rio de Janeiro: Ministerio do Trabalho, Industria e Commercio, Instituto Nacional de Tecnologia, 1957.) [191

World Health Organisation. Technical Report Series. No. 149: Joint FAO/WHO Expert Committee on Nutrition—Fifth Report. Pp. 55. 2 Swiss francs; 3*s*. 6*d*.; 0.60 dollars. No. 153: Insect Resistance and Vector Control—Eighth Report of the Expert Committee on Insecticides. Pp. 67. 2 Swiss francs; 3*s*. 6*d*.; 0.60 dollars. No. 157: Air Pollution: Fifth Report of the Expert Committee on Environmental Sanitation. Pp. 26. 1 Swiss franc; 1*s*. 9*d*.; 0.30 dollars. No. 158: Expert Committee on Medical Rehabilitation—First Report. Pp. 52. 2 Swiss francs; 3*s*. 6*d*.; 0.60 dollars. (Geneva: World Health Organization; London: H.M. Stationery Office, 1958.) [191

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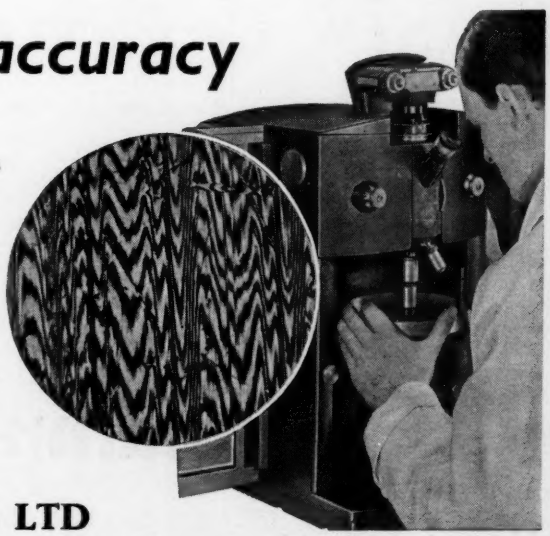

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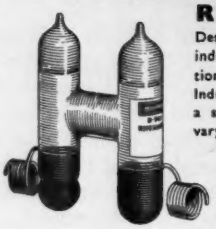

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